

Science & Cents



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Science and Cents

On April 19, 2002, the Federal Reserve Bank of Dallas hosted a conference, Science and Cents, Exploring the Economics of Biotechnology, which Mine Yücel and I organized at Bank President Bob McTeer's urging. Understanding the economics of biotechnology is important partly because biotech will likely be one of several future growth industries and more significantly because advances in this area will affect the well-being of people throughout the world and for many years to come. Today's presentation reviews some of what we've learned from our ten conference speakers, focusing on the following issues:

- (1) the potential economic gains from biotech;
- (2) the hurdles to R&D-particularly costs, capturing returns, and financing; and
- (3) the broader implications surrounding these issues.

Unfortunately, time constraints do not allow me to cover other issues, such as the science behind biotech and nano-technology, topics on which Malcolm Gillis and Tom Caskey spoke eloquently at the conference, or biotech's impact on agriculture, something not addressed in the conference. In the future, the other conference organizer, Mine Yücel, could address some other biotech issues, including the regional impact of biotech and what Texas can do to further foster biotech activity.

Before proceeding, it may be helpful to quote the *American Heritage Dictionary's* definition of biotechnology as, "the use of micro-organisms, such as bacteria or yeasts, or biological substances, such as enzymes, to perform specific industrial or manufacturing processes," and more broadly, "the application of the principles of engineering and technology to the life sciences." In recognition that there are many technical terms in this presentation, I have included a glossary at the end of this document.

The Potential Economic Gains From Biotechnology

The Big Picture

On the issue of the economic gains posed by biotech, our first speaker, Professor Michael Darby of UCLA, emphasized that biotech research appears to represent a major, metamorphic revolution in which new industries are created, rather than the type of incremental progress that perfects existing products. As with earlier technological revolutions, our ability to track or gauge biotech's importance is hampered by a lack of data and history. Another trademark of a metamorphic revolution is that many new firms enter an emerging industry that has few or no incumbents. And very few of these new firms succeed. Within biotech, only about 10-20 percent of early firms became large.

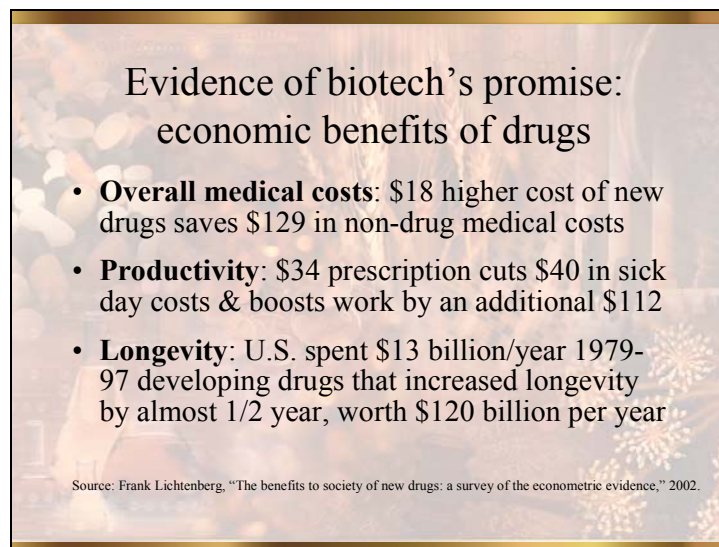
Potential Gains: the Case of Pharmaceuticals

Our second speaker, Professor Frank Lichtenberg of Columbia University, discussed some of the limited evidence on biotech's promise from studies of the economic benefits of drugs. These benefits take the form of lower overall medical costs, higher productivity, and increased longevity. Recently the press has paid much attention to rising drug costs. But as the great French economist Frederic Bastiat emphasized, economists should consider what is unseen, not just what is seen. In the case of pharmaceuticals, the press has left many of the benefits unseen.

For example, with respect to medical costs, what is seen, the \$18 dollar higher cost of new drugs per person is more than offset by what is unseen or less well-seen: namely, a \$129 dollar estimated decline in net, non-drug medical costs. These savings mainly stem from new drugs eliminating or shortening hospital stays by being more effective than older drugs.

In addition to these cost savings, there are gains from boosting worker productivity. In particular, econometric studies by Lichtenberg estimate that for every \$34 spent by employers and their employees on prescriptions, the cost of sick days falls by roughly \$40. And if society factors in how drugs can help the disabled work or perform better, there are additional gains of \$112. Together, these estimates imply that \$34 spent on prescriptions has boosted productivity by roughly \$152. Of course, these findings are based on past experience and there is no guarantee that future prescriptions will pay off as handsomely.

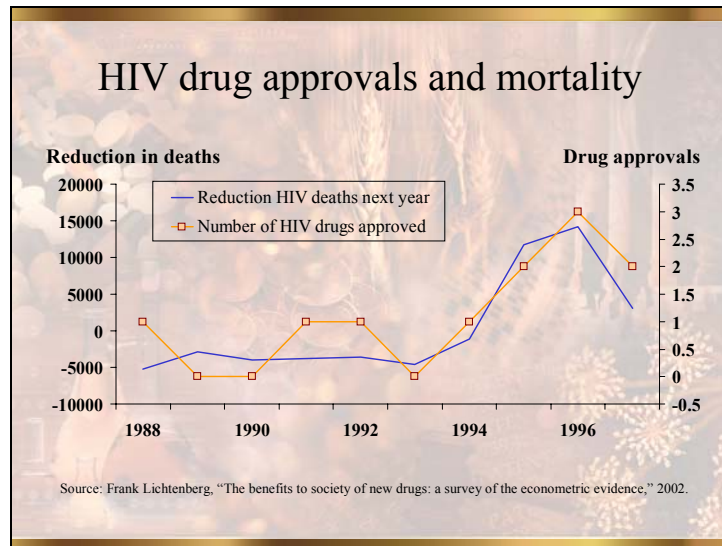
Figure 1



Another major benefit from pharmaceuticals arises from increased life expectancy. Between 1979 and 1997, the United States spent an average of \$13 billion a year on developing new drugs which have collectively boosted longevity by 0.4 years, according to economic research. As noted by Lichtenberg, this impact on life expectancy, almost one-half year on average, is worth about \$120 billion a year using one economic yardstick.

One striking example regarding longevity concerns the impact of new drugs on HIV mortality. As shown in Figure 2 below from Professor Lichtenberg's conference paper, the pace of new HIV drug approvals—shown in blue—has a striking correlation with the reduction in HIV deaths in the following year, shown in brown. To a large extent, the surge in HIV drug research and approvals was enabled, or at least sped up, by the Orphan Drug Act of 1983. This legislation cut much of the red tape in the drug approval process for pharmaceuticals designed to treat or prevent rare diseases or diseases for which the economic returns to the private sector would otherwise be insufficient to cover research and development (R&D) costs.

Figure 2



Hurdles to R&D

In light of biotech's great promise, we need to understand and overcome the hurdles to biotech research, which were addressed in our conference. These hurdles include:

- (1) the high risk of biotech R&D;
- (2) the high and rising costs of R&D, both of which are analyzed using data on the biotech industry with the longest track record, drugs;
- (3) the difficulties firms have in capturing the returns to their inventions; and
- (4) funding biotech research, particularly with respect to venture capital and the role of the public sector.

High Risk as a Hurdle to R&D

Perspective on the risks and costs of drug R&D was provided by Duke University Professor Henry Grabowski. One of the biggest hurdles to drug research is its high risk. As noted by Professor Grabowski, historically only 22 percent of drugs that enter clinical trials pass and get FDA approval. Furthermore, even among the approved drugs there are few winners, as evidenced by three facts. First, only one-third of approved pharmaceuticals have covered out-of-pocket expenses, which are not adjusted for time or risk. Second, the top 20 percent of new drugs according to revenues out-sell all the other 80 percent of new drugs combined. And third, earnings at large pharmaceutical companies are mainly from a few drugs, in some cases just one or two.

High and Rising Costs as Hurdles to R&D

Two other important hurdles to drug research are that R&D costs are high and are rising at a fast pace. Professor Grabowski and his co-authors estimated that it costs about \$400 million dollars in out-of-pocket expenses to develop a new drug. In addition, we should also account for the lengthy 10-12 year gestation period needed to develop a drug, along with the high risks. Adjusted for risk and time, these researchers estimate that it costs roughly \$800 million to develop a new drug.

Also of concern is the pace of R&D cost increases, which exceeded the pace of inflation in the 1980s and likely in the 1990s. Older data show that clinical cost increases accelerated during the 1980s, rising at nearly a 12 percent annual pace, up from about 6 percent in the 1970s. Despite a slowing of nonclinical cost increases, overall R&D cost increases only outpaced overall inflation by roughly 7-1/2 percentage points on an annual basis in the 1980s, after outpacing inflation by a slightly smaller 7 percentage points (on an annual basis) in the 1970s. Incomplete data indicate that this outpacing of inflation and the acceleration of clinical costs likely continued in the 1990s. Especially troubling in this regard is the doubling of the length of clinical trials from 33 months in the 1980s to 67 months today.

Capturing the Returns of R&D as a Hurdle to R&D

In light of the high and rising costs of biotech R&D, inventors need to capture enough of the economic returns. In general, biotech firms defend their intellectual property through formal patents and an evolving set of new legal strategies.

With respect to the former, there is an important balancing act. Because R&D costs and risks are high, patents need to be long enough for firms to recoup their risk-adjusted R&D costs, without unduly dissuading patent holders from conducting more research. We should also note that patents provide outsiders with information about new discoveries which, in turn, spurs more research. As emphasized by Professor Grabowski, patents are the most important factor affecting R&D decisions in surveys of biotech firms.

The main reason is that R&D for new drugs differs from that of imitating existing drugs via generics in three dimensions. First, the out-of-pocket costs of developing a generic are only one to two million dollars, far below the 400 million for developing a new drug. Second, the clinical success rate for generics is 90 to 100 percent, four to five times that of new drugs. Finally, it only takes one to two years to develop a generic versus 10 to 12 years for a new drug.

But earlier, established patent practices may not be enough. As emphasized by Rebecca Eisenberg, a law professor at the University of Michigan, the rapid evolution in biotech science has led to a rapid evolution in patent strategies because it takes a while for law to catch up with science. In particular, innovators are pursuing strategies to claim a share of the value of future products, which were developed using their inventions. These include pursuing licensing agreements that allow others to use one's invention in exchange for a share of future products and pursuing damage awards from the unlicensed use of an invention that has already led to the development of a profitable product. Partly to avoid the costs and hassles of these two approaches, another strategy is to seek patents that explicitly cover future discoveries enabled by prior inventions.

Funding Biotech Research

Funding expensive and risky research is another hurdle. Outside of pharmaceutical research, which is often done by established drug companies, much biotech research is conducted by new firms, which are often partly funded by venture capital firms and other private equity investors. Much of their applied research is based upon basic or generic research that is either publicly funded or conducted at publicly funded universities and other institutions. Given that future biotech research is likely to branch out beyond old-style pharmaceutical R&D, our financial speakers focused on the roles played by venture capital and the public sector.

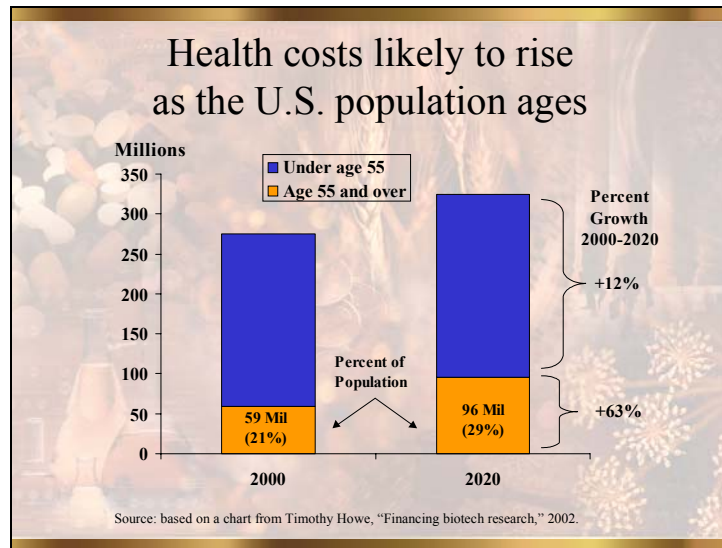
Venture Capital

One of our speakers, Tim Howe, who co-founded a medical venture capital fund and who teaches venture financing at Columbia University, emphasized several points about the role of venture capitalists. First, biotech venture capital firms combine managerial with scientific talent in picking, funding, advising, and even managing biotech start-ups. By performing these roles, venture firms enable scientists in start-ups to focus on inventing. A second point is that most venture firms make direct investments in young companies, without intermediaries, and the distribution of returns is highly skewed, with few big winners.

Another important aspect of venture capital firms is that they have an incentive to diversify across solutions to medical problems, which can be found not only in biotechnology, but also in medical devices and service firms. Finally, the rising share of GDP devoted to health and the related-aging of the baby-boom generation pose big incentives for venture capital firms to enter the medical arena.

Building off a figure from Timothy Howe’s presentation, Figure 3 below plots the overall U.S. population, with the age 55 and older group broken out using the lighter colored bar portions. While the overall population is projected to grow at a modest and steady rate, we can see that the 55 and over crowd is projected to increase from 21 percent of the population, given in parentheses, to 29 percent by 2020. As shown at the extreme right, the older population is expected to grow by 63 percent over these two decades, five times the 12 percent rise in the younger age group. This is important because the older group spends much more on health; for example, people 55 and over spend an average of 3 times more days in the hospital than do younger folks.

Figure 3



With respect to the future, our speaker saw two general sources of opportunities for venture capital. The first concerns a shift in the type of science funded. Venture firms focused on funding conventional drug development in the 1980s and genomics in the 1990s. Looking ahead, venture firms are likely to fund projects in proteomics, the study of how human genes produce proteins that act upon the body. The human genome project has identified over 35,000 genes, but current drugs work on only 400 proteins. Although proteomics is much more complicated than genomics, it offers the benefits of customizing drugs, which would help reduce the toxic side-effects of drugs by tailoring treatments to one’s genetic make-up with an eye toward affecting the body’s output of proteins.

Timothy Howe sees the other big opportunity in the maturation of the oldest, most established biotech industry, pharmaceuticals, from a vertically integrated industry to a horizontally organized one. He likened the drug industry to the computer industry of twenty years ago, which was dominated by big vertically integrated firms like IBM, DEC, Sperry-Univac and Wang. Two decades ago, those firms did it all, from manufacturing chips and computers, to designing application systems and software, and to selling and distributing their products. Since then, the computer industry has been transformed into a horizontally integrated industry with a few big players dominating each particular segment. For example, we can see the emergence of segment leaders such as Intel in chips, Hewlett-Packard-Compaq and Dell in personal computers, and Microsoft in operating systems and software. Similarly, Tim Howe sees the pharmaceutical industry becoming dominated by a few major players in distinct horizontal segments, such as research and target discovery, clinical testing, and distribution.

The Public Sector Role in Funding Biotech Research

Now let's turn to the public sector's role in financing biotech research and the points made by Professor Michael Lawlor of Wake Forest University. Historically, the returns to R&D have exceeded those on other investments. At the macroeconomic level, U.S. economic growth has arisen more from innovation than directly from growth in the capital stock or labor force. And at the microeconomic level, most studies find that inventors recoup but a part of the economic value of their research.

But if the returns are so large, why hasn't there been more investment, which would drive the returns down to normal? One reason is that there are high risk premia on biotech investments since there are few winners. Another is that inventors don't get to keep all the economic value generated by their discoveries which spills over to others.

There are three public policy options to addressing under-investment, each with its own drawbacks: industrial policy, tax credits, and direct funding. By investing directly into researching and producing goods, an industrial policy poses the problems stemming from state enterprises operating in a dynamic area. Tax credits sound appealing, but it is hard to prevent firms from reclassifying other expenses as R&D, thereby diluting the effectiveness of a tax cut. The other option is directly fund R&D, but this runs the risk of mismanagement if there is too much political interference or not enough accountability in selecting which research projects to fund.

As Professor Lawlor stressed, a complex, direct funding approach has evolved in the U.S., helping make us the world leader in biotech research. He began by noting that the public role in R&D surged in WWII when the federal government boosted its direct funding of research, with projects ranging from the Manhattan project to perfecting the mass production of penicillin. After that war, federal funding of health research focused on basic research, that was driven by curiosity and war-time concerns linked to security and politics, and was not directed much at applied research driven by commercial considerations.

During the early years of the Cold War, funding was greatly expanded for the National Institutes of Health (NIH). The NIH is a hybrid institution whose social mission is set and funded from the top, but whose operations are largely not hindered by excessive centralization. Congress sets NIH's budget, but scientists select NIH research projects from many applications in a careful peer review process. This allows for accountability, flexibility, and competition.

In recent decades, public funding of R&D has evolved in response to the increased complexity of research which is more interdisciplinary and which has blurred the lines between basic and applied research. In particular, generic technology development has become more important as new technologies are becoming applied in more fields, hence the adjective, "generic."

In recognition of these trends and in an attempt to encourage the transfer of federally funded research to the private sector, Congress passed legislation in the mid-1980s that created cooperative research agreements (CRADAs). These CRADAs allow federally funded laboratories to establish research links for their own profit with commercial firms using their lab results. In addition, the Department of Commerce instituted the advanced technology program in 1990 to directly fund research into developing new generic processes for high tech industries. This program, known by its acronym, ATP, has been instrumental in speeding up and reducing the risk of research in stem cells, regenerating human tissue, and treating diabetes.

Broader Implications

To conclude, let's examine several, but not all, of the broad implications of biotech. First, at a time when health care premiums are growing very rapidly and drug cost increases are getting much press, we should remember that the benefits of new drugs have historically greatly outweighed their higher costs. So employers should think hard before restricting drug benefits as a means of holding down medical costs.

A second broad implication is that policymakers should appropriately spur basic and generic research. With respect to funding, it is encouraging that NIH's budget for next year is twice what it was in 1998. But we need to be careful that interventions in the form of price controls or forcing pharmaceuticals to relinquish property rights could reduce the incentives for innovation. Given the high cost and risks of biotech research, emerging industries need a few big winners to justify investing in many new ideas. And patent and royalty laws need to catch up to the technology so that the markets can perform better.

In addition, there are direct and indirect implications for investors. Direct ones include recognizing that there are very high risks of holding large portfolio stakes in individual biotech firms. In addition, excluding pharmaceutical makers, biotech stock indexes have very high valuations, suggesting that this sector may be over-valued. Given the difficulties in capturing the value of inventions, investors should consider the risk that innovations could benefit end-users more than inventors.

Perhaps the biggest implications for investors arise from the indirect effects of biotech research on benefit costs and customer bases for all sorts of companies. In particular, the population could age more than projected if biotech research greatly boosts longevity. As a result, firms with large defined benefit pension obligations could face greater risks, as would the Social Security retirement system. On the other hand, medical advances might help control the projected jump in Medicare benefits, which are seen as producing bigger budget shortfalls than the looming social security retirement problem, as Professor Tom Saving of Texas A&M pointed out last December to this board.

Another demographic implication is that spending patterns could shift more if the population ages more rapidly than expected, particularly if medical advances reduce disabilities and improve the quality—as well as the quantity—of life.

These are just some of the economic implications of biotech, and I have shared only a part of what we learned from our conference. The papers and slides from this conference, including Malcolm Gillis' wonderful luncheon address, are posted on our web site, www.dallasfed.org. Other important aspects of biotech include the regional impact of biotech and what Texas can do to encourage the growth of emerging, biotech industries. These are topics that my conference co-organizer, Mine Yücel, could address in a future presentation.

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Short Glossary

Advanced Technology Program (ATP): the Department of Commerce instituted the advanced technology program in 1990 to directly fund research into developing new generic processes for high tech industries.

Biotechnology: “the use of micro-organisms, such as bacteria or yeasts, or biological substances, such as enzymes, to perform specific industrial or manufacturing processes,” and more broadly, “the application of the principles of engineering and technology to the life sciences,” American Heritage Dictionary.

Clinical Trials: the phase of R&D where the effectiveness and safety of a product is tested.

Cooperative Research Agreements (CRADAs): agreements under which federally funded laboratories can establish research links for their own profit with commercial firms using their lab results.

Genomics: the scientific discipline which systematically investigates the set of chromosomes and genes of an organism.

Gestation Period: in the context of biotechnology, this refers to the period during which a product is being researched and developed, not including the development of prior technologies used in the research.

Incremental Progress: the type of technological progress in which an existing product is perfected or the process of making that product is perfected.

Nanotechnology: a diverse group of new technologies operating on the scale of atoms and molecules, specifically in the range of 0.1 to 100 nanometers, a nanometer being one millionth of a millimeter.

Non-clinical Costs: the R&D costs incurred outside of the costs of clinically testing a product.

Proteomics: the use of quantitative protein-level measurements of how genes behave and affect the body.

Stem Cells: cells that can develop into many different types of tissue and could be the key to a number of therapeutic breakthroughs in the field of medicine and research.

Venture capital: private equity capital invested in a new or fresh enterprise.