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Summary: ***Critics claim the pharmaceutical industry is unique and therefore requires distinctive forms of regulation, such as price controls. But absent in this view is a systematic appraisal of the economics of the industry. Were their approach adopted, the consequences would be less innovation, fewer life-saving drugs, and a less-healthy citizenry than what could be possible.***

ISSUE BRIEF

Does America Have a Prescription Drug Problem?

The Perils of Ignoring the Economics of Pharmaceuticals

By Richard A. Epstein

Introduction

It is a sign of the times that two recent critiques of the pharmaceutical industry have been published, both under the title "America's Other Drug Problem"—equating, in essence, the lifesaving benefits of the pharmaceutical industry with the seamy and destructive world of illegal drugs.

The purpose of these two studies, one by Public Citizen and the other by two eminent physicians, Drs. Arnold Relman and Marcia Angell, is to challenge the way new pharmaceutical drugs are developed and marketed.[1]

The short-term sources of discontent from which these two publications draw strength are both simple and powerful: prescription drug prices are high, and getting higher; but they also are subject to wide price variation within the United States and across different countries. These price differentials create a general perception of unfairness, and they spur multiple efforts to arbitrage the markets by shipping drugs from locations in which they can be bought relatively cheaply to those in which they are more expensive.

As a result, even those who normally understand the economic benefits of differential pricing are wavering. Senator Trent Lott (R-Miss.), for example, now supports legislation that would allow importation of foreign drugs.

"I can't explain to my mother," says the senator, "why she pays twice as much for her drugs" in the United States as they cost elsewhere.[2]

Any single dramatic price increase, such as the fourfold increase for Norvir, provokes widespread cries of indignation and calls for patent invalidation or new forms of state regulations.[3] Moreover, talk of price controls for patented pharmaceuticals is bandied about, even by individuals who know better, are uneasy about the prospect of their arrival and would summarily reject price controls on other products.[4]

Calls for special treatment [of the pharmaceutical industry] should go unheeded—otherwise, we will pay the price in poor-quality drugs and lower rates of innovation.

Time and time again, critics claim that the "special" nature of the pharmaceutical industry calls for distinctive forms of regulation that would be regarded as improper elsewhere. But in most cases these calls look simply like disguised efforts to reduce the levels of innovation in a highly successful industry, whose major problem lies in the regulatory cloud that hangs heavy over its head. An examination of first principles shows that these calls for special treatment should go unheeded—otherwise, we will pay the price in poor-quality drugs and lower rates of innovation.

Back to the Future: Socialism or Capitalism—or Both

The current debates bring back in microcosm the long-standing debate over the proper organization of the means of production and distribution of goods and services. Although the participants in today's debate tend to view their efforts as an exercise in current events, they actually hearken back to the long-simmering dispute over the respective merits of capitalism and socialism that occupied central stage in the first half of the 20th century. That debate was directed toward two issues that constantly recur today:

- Who should own the means of production, the state or private individuals?
- What is the ideal means of distribution of wealth derived from that production?

In tackling these issues it is easy to identify two extreme positions that surround an array of intermediate possibilities. At one end of the spectrum lies the socialist dream that insists that it is possible to have the best of both worlds: to use a system of government-run centralized planning to ensure that all resources are put to their highest-value uses, and then, independently, to adopt an equal-income policy on the grounds that a dollar of wealth is worth more to a poorer person than a richer one.[5]

On the other side of the debate lies capitalism, which insists that only a decentralized system of prices can supply the information that allows independent traders and entrepreneurs to decide which investments to undertake and which ones to avoid.[6] In this view, inequalities of wealth are needed in order to generate the economic vitality that in the end will redound to the benefit of individuals across the income spectrum. This market-oriented view of the world leaves, of course, an important role for government insofar as it provides social order and the physical and legal infrastructure that is needed for the operation of markets. The laissez faire model, as it were, is treated as tantamount to anarchy only by its opponents, never its supporters.[7]

As a matter of general economic history, notwithstanding its distinct echoes in the current debate over pharmaceutical policy, in its extreme form socialism as a general political philosophy today has few if any friends. The problems of political incompetence and corruption are so endemic to any system of state-run enterprises that nations throughout the world have systematically sought to privatize their major industries in a slow but inexorable move toward market liberalization—one notable exception being the U.S. health care system.

Even the most once-ardent socialists have abandoned any claims for the superiority of government-owned businesses, and have instead put their faith in systems of state regulation that exert some control over the types of goods produced, and the prices for which they can be sold in the marketplace.

The key questions today, therefore, do not concern the stark choices between capitalism and socialism that dominated the intellectual landscape more than half a century ago. Today's pale shadow of socialism finds its most powerful expression in New Deal-like efforts to regulate those markets that are thought to be subject to inequalities of bargaining power. For example, the labor markets are subject to minimum wage requirements, collective bargaining statutes and antidiscrimination laws, which are opposed by those, like me, who work in the free market tradition.[8]

Outside of labor markets, the struggle between market institutions and regulation more often than not takes place on an industry-specific basis. In this context, the strongest case for regulation involves those goods and services that are most efficiently provided by a natural monopoly, that is, an industry in which the cost of supplying an additional unit of service is declining over the relevant domain, so that a single supplier can furnish goods at the lowest cost to all comers.[9] Public utilities, transportation and telecommunications have been the traditional industries that have fallen into this class, but the history of regulation in these areas has been spotty at best.[10] And the regulations continue to give rise to major litigation to this very day.[11]

The Extraordinary Pharmaceutical Industry

This debate over regulation has spilled over into all aspects of the health care industry, including the longstanding debate over whether some form of universal health care is preferable to a system of unregulated markets, or the ungainly mixed system that combines some form of regulation with extensive levels of subsidy through Medicare and Medicaid.

I shall sidestep that huge debate and confine this analysis to the pharmaceutical industry, which has become the lightning rod in the debate over the nature and function of regulation.[12] In particular, I shall focus on the Relman/Angell broadside, backed up as it is by the work of Public Citizen.

In speaking about the pharmaceutical industry as this nation's second drug problem, neither source pauses to speak about the benefits to life and health that have come from pharmaceutical innovation.[13] Instead, they concentrate all their considerable endeavors to explain why this nation should redouble its effort to rein in the industry.

The effort of Relman and Angell to set up the welfare of the firm does a disservice to the consumer interests that they seek to protect.

The Relman and Angell critique merely updates vintage socialist arguments by insisting that while for-profit firms may perform a useful social function in "ordinary markets," they should not be allowed to dominate in areas as sensitive as health care. They argue that "the market for drugs is not like other markets." Thus, it is dangerous to allow the policies of for-profit innovator drug companies to be "impelled primarily by the financial aspirations of their investors and executives."[14]

It is evident that this worldview extends the legitimate scope of state regulation of private firms beyond the control of harmful externalities (e.g., pollution) or monopoly, which market-based proponents agree are a legitimate sphere for government action. But their arguments go further, embodying at least two common misconceptions that need to be exposed before considering the particular charges.

Misconception #1: Drugs Are Not Like Other Products. The first of these misconceptions is the undefended assertion that the pharmaceutical industry is not like ordinary markets. That common but dangerous ploy is used in virtually every modern instance to expand the scope of regulation over the goods and services that firms supply to markets.[15] Thus:

- The extensive forms of price regulation for farm goods is justified on the grounds that food, which is necessary for survival, cannot be left to the operation of the market, especially if the competitive forces that bring lower prices might also result in the bankruptcy of some farmers, which they always will.
- Rent control is justified on the grounds that housing is also a unique good and without it people would be left homeless in the streets.
- The extensive regulation of labor markets is also predicated on the socialist belief in the pervasive nature of market failure.[16]

But in each and every case, the network of regulations in question has produced more harm than good by adding frictions to the operation of a whole range of economic systems and distorting the behavior of individuals and firms as they maneuver either to avoid the regulatory sweep or to gain its protections.

Such broad claims of failure should always be required to show a specific evil that regulation is able to combat, without introducing greater evils of its own. It is on that ground that regulation for safety and efficacy under the Food and Drug Administration has been justified, and it is on precisely that means-ends correction that regulation is subject to attack, which may call for a streamlining, instead of an elimination, of the entire regulatory apparatus in an effort to speed new drugs to the market. Thus, the insistence that pharmaceuticals are not "ordinary goods"

rises to the level of theology because it is based on preconceived beliefs rather than evidence, which is hardly the way to proceed in this dispute.

Misconception #2: Drug Companies Only Want to Maximize Profits. There is of course *no* business that does not wish to maximize the income of investors and employees of the firm. But it hardly follows from that commonplace observation that firms will succeed only by a single-minded devotion to this parochial end.

The great intellectual achievement of Adam Smith in the *Wealth of Nations* was that he showed that within the framework of a competitive industry, the firm that sought to maximize its profits would also maximize overall social welfare. Under competition all goods that are worth producing are produced, while those whose costs exceed their benefits are not. The ability of consumers to enter and exit the market is the only constraint that is needed to make sure that the for-profit firm is attentive to the interests of its customers.

Indeed, the constant effort of Relman and Angell to set up the welfare of the firm in mortal opposition to consumers does an enormous disservice to the consumer interests that they assiduously seek to protect. A firm is not some disembodied entity that has utility or wealth of its own. It is a collection of individuals, both investors and creditors, who put up money in the expectation of a return that will compensate them for the risk of the business that they enter.[17] A system of price regulation that denies that return will lead them to exit the business in question, which will only work to the long-term disadvantage of the consumers who so desperately need the products and services.

Popular sentiment has shifted against the [pharmaceutical] industry…

It is easy to demonstrate that any imposition of price controls leads to an excess of demand over supply at the artificially set price, creating shortages in the short run and investment dislocations in the long run. On this question at least, there is nothing unique about the pharmaceutical industry relative to any other. Starting from the global assumption that profit-making firms should not be entrusted with important components of health care regenerates the specter of the socialist case for centralized planning. What the authors need to do is explain why and how "the drug industry distorts medicine and products."[18]

Instead, Relman and Angell mount a three-front attack on the practices of the pharmaceutical industry. The component that I shall emphasize here looks at the various practices in the development, pricing and marketing of patented prescriptions. Since space does not permit, I shall not address in any detail the many issues that concern the role of the Food and Drug Administration in the regulation of prescription drugs. Nor shall I address the distinctive patent questions that arise in the pharmaceutical area, many of which concern the interaction between the patent system and health and safety regulation under the FDA.[19]

In dealing with these various drug development and marketing issues, it would be foolish to advance any claim of perfection for the pharmaceutical industry, which has surely made its fair share of errors. The truth is that overall popular sentiment has shifted very much against the industry so that there are few issues today on which it could hope to get a fair hearing, as those other "ordinary" industries might.

Rather, the pendulum has swung strongly in the opposite direction. The proposals for legislative reform, such as various price control and importation schemes, all tend to find ways to reduce the ability of firms to run their own affairs, to subject them to greater scrutiny under the FDA and limit the duration and strength of their patents. In most instances these reforms, many of which are championed by Relman and Angell, are off the mark. But the issue demands individuated examination of the charges leveled against the industry and the proposals for reform.

Free Markets *and* a Commitment to Care

All proponents of socialized medicine routinely bewail the amount of money the U.S. spends on health care. And they want to blame the pharmaceutical industry for it. But the truth is that huge components of the overall national health care budget are attributable to matters that are wholly outside the scope and control of the pharmaceutical industry, or any other health care industry, for that matter.

Total U.S. health care spending is shaped in large part by an extensive national commitment to treat health care as a "right," regardless of the individual's ability to pay. That general commitment rests in part on the basic ethical conviction (which I do not wish to dispute) that wealth is a poor proxy for utility in contexts that involve life or death issues.[20]

The inability to pay for treatment does not mean that a person whose life is at risk has no intrinsic social worth. Indeed, the entire system of charitable care in the U.S. and elsewhere grew up with the explicit recognition that a standard of "willingness to pay" is insufficient.

There is, alas, no easy fix to this serious problem, for the effort to supply all health care without regard to market constraints creates a second and larger problem: no one has ever found an effective means to ration the amount of health care provided. As a result, individuals who are spared the need to pay for their health care services will consume excessive quantities—more, in fact, than they would purchase if they had sufficient funds of their own to spend as they please.

If an extra dollar spent on pharmaceuticals reduces the need for other treatments that pose a greater risk, then increased pharmaceutical spending is a social good.

There are of course no free lunches. The insistence on a right to health care generates a full range of subsidiary issues, of which I shall consider here the following:

- Rates of drug utilization and the role of price discrimination in the market for patented pharmaceuticals;
- Price movements of individual drugs;
- The respective spheres of public and private support for drug innovation;
- The place of "me-too" drugs;
- The role of advertisement in drug pricing; and,
- The cost of research for new wonder drugs.

All of these themes meld together because, once the standard principles of business and economic analysis are understood, the practices of the pharmaceutical industry look much less out of whack than their critics suppose.

Rates of Drug Utilization

Relman and Angell launch their initial salvo on the pharmaceutical industry by appealing to the common perception that the U.S. spends a lot on prescription drugs—about $170 billion per year, which is in line with general estimates—and complain that it is a rapidly growing fraction of the national health budget of $1.4 trillion. They write: "Greater overall use of drugs, higher prices for new drugs, and steady increases in the prices of existing drugs all contribute to an annual inflation rate in drug expenditures of 14 percent (down from a high of 18 percent in 1999)."[21]

This general criticism, which lumps together several disparate elements, offers an accurate thumbnail description of the current marketplace. But it does not in and of itself supply the needed indictment of industry practices.

In response, it should be noted that these price increases are not uniform over all periods. In contrast with the account offered by Public Citizen, the Pharmaceutical Research and Manufacturers of America (PhRMA) notes that the increase in retail prescription drug prices was only about 1.5 percent in the period between November 2003 and March 2004.[22]

But the broader criticism, especially by champions of a system of universal health care, cannot depend on a charge that the pharmaceutical industry is grabbing an increasing fraction of the health care dollar.

To see why, recall that before any pharmaceuticals were on the market, the industry fraction of expenditures was zero. Clearly, the initial set of increases was most welcome because it provided avenues of relief that could not be as easily met by other means. The same dynamic continues to this day.

The issue isn't whether we are spending more on pharmaceuticals as a percent of total health care spending; the issue is whether we get more value for a dollar spent on pharmaceuticals than a dollar spent on other types of health care. Thus, if an extra dollar spent on pharmaceuticals reduces the need for other treatments (e.g., surgery) that pose greater risk and promise smaller benefits than drug therapy, then increased pharmaceutical spending is a social good.

Second, the new treatments could shorten recuperation time and lower overall expenditures on medical care.

While patients may enjoy and appreciate the benefits of less-invasive therapy, shorter hospital stays and a better quality of life that may come with increased prescription drug use, the cost savings are not easily recognized or calculated. Thus critics such as Relman and Angell can bemoan pharmaceuticals' growing share of the health care dollar with impunity because discerning the benefits to patients and health care costs is so difficult.

Neither of the two critiques addresses the social consequences of this substitution toward drugs. Nor are there any independent reasons to believe that the greater expenditure on drugs represents some systematic decline in social welfare. *Indeed, in many cases the most common criticism is that treatments are not made available to individuals who are in a position to benefit from them, which suggests that the level of drug expenditures is as likely to be too low as it is too high.*

It also makes it all the more inexplicable that Relman and Angell are strongly opposed to direct-to-consumer advertising, which offers some hope of reaching patient populations in need who are unable to make regular trips to the doctor.[23]

Price Discrimination

In the United States there is no single price at which any patented or off-patent drug is sold. Drugs are sold to numerous types of purchasers, often at different prices, and often with rebates that are not publicly announced.

Successful innovator companies are granted the exclusive right to sell their patented products, creating a short-term monopoly, but only if there are no close substitutes for the patented product. The problem they face is determining what is a reasonable price for a product with few or no substitutes, especially when the price can become a political as well as an economic issue.

The Innovator's Dilemma. The basic problem faced by the holder of the patent is determining how much to charge for each unit that it sells. One possible method is to charge each person the cost for the marginal production of each additional unit that comes to market. Here it is generally the case that the initial pill will have very high costs—how much is an issue to which I shall return in a moment—while the subsequent pills could be produced for a tiny fraction of that initial cost.

But pharmaceutical drug manufacturers incur extensive research and development costs, with clinical trials and regulatory approval, before a *single* pill is offered on the market. Everyone, therefore, is keen to pay for the *second* pill, but no one wants to pay for the *first* one. But unless someone is willing to pay for the first pill, the second will never be produced, and so no one benefits. Yet it is clear that no potential user of the patented drug is better off in a world in which the drug is simply not available relative to one in which it is available, albeit to some at a very high cost.

This problem of high-fixed, low-variable cost has long been recognized as a fundamental objection to the competitive market of a laissez faire system.[24] The harder question is what to do about it. On this point, the only feasible, if imperfect, solution is one that shifts some of the cost from the initial user and places it on subsequent users. For this system to work, however, it is necessary that all subsequent users pay enough *above* the marginal cost for their own pills to cover the cost of initial production over the drug's limited lifetime.

That solution creates an inefficiency of its own, because now the higher price for the subsequent pills means that some people will be forced to do without the new treatment even if they can afford to pay the marginal cost of production. The point here is not new and has come up in other contexts with other sorts of monopolies.[25]

Since no one wants to pay for the first pill, that cost has to be spread out over other users.

It may cost $1 million to build a bridge that is *costless* to maintain. To charge nothing for its use means that tax revenues (which create distortions in other markets) have to be used to fund the construction of this bridge, raising the risk that pork barrel politics will lead to the construction of many bridges that should never be built at all.

How to Handle "First Adopters?" This same set of insights applies to the patent area.[26] Since no one wants to pay for the first pill, that cost has to be spread out over other users. But there is no unique way in which that allocation can be made because each potential buyer will seek to pay as little of it as possible.

One possibility is to constrain the holder of a patent so that it must charge a uniform price to all users. That price can be set above marginal cost and might well allow the patentee to recover its front-end costs. But that system has the unfortunate side effect that any individual who can afford to pay something above the competitive price but below the monopoly price is shut out of the market, while very high demanders (often individuals with great wealth) are allowed to reap a substantial consumer surplus (i.e., a high difference between their willingness to pay back in dollars and the price they are charged).

In practice, therefore, some measure of price discrimination may well both increase the profits of the patentee

and improve social welfare simultaneously by seeking to charge everybody a uniform price that is just below the maximum prices that they are prepared to pay.

One Market Response. But just how does that discrimination manifest itself in the market? In practice, it turns out that large health benefit plans have an advantage over ordinary consumers (whose prices appear to be the concern of Relman and Angell; they are not, however, explicit about the consequences of market segmentation).

The health plans with their own dispensaries are able to go to the supplier of a given drug for which there is a viable competitor and say that unless it gets rock-bottom prices it will shift its entire purchase order to a rival. Often both parties will keep the rebate secret, for the buyer knows that if the information becomes public, its size will perforce be reduced, as the manufacturer may be forced to offer a like deal to other firms.

Some measure of price discrimination may well both increase the profits of the patentee and improve social welfare simultaneously…

In contrast, the ordinary pharmacy has to stock a full line of products for its wide range of individual customers and thus does not have that flexibility. But any system of state-imposed price controls that required all firms to give "most favored nation" treatment to all individual users would not increase overall efficiency. The lowest prices would start to rise, which would cut some individuals out of the market, while the high demanders would receive the benefit of lower prices. It follows, therefore, that some form of price discrimination is necessary to keep the pharmaceutical markets viable, and will emerge without any form of collusion among manufacturers in violation of the antitrust laws.[27]

In light of this helter-skelter system of industrial organization, there is no single "price" at which any drug is sold. Further, the problem becomes more acute when foreign markets are thrown into the mix, for as Relman and Angell rightly note, prices in the U.S. are higher than they are elsewhere in both developed and undeveloped nations, by amounts that vary between 50 percent and 64 percent.[28]

The Impact of Other Countries. These striking price differences reflect, however, not only the inveterate need of patent holders to engage in price discrimination to recover their fixed costs, but also the stated policies of foreign governments to set the prices at which drugs are sold in their country. This is easily implemented in those nations like Canada where there is only a single national health care service, which can now act as a monopsonist (i.e., a situation where there is one large buyer) that will get its way. So long as the foreign nation is willing to bite off some portion of the fixed cost, no supplier is willing to abandon that market, at least if it is confident that goods which are sold in that country will not be resold elsewhere.[29]

But for many reasons it is pointless to protest these developments as well. There is nothing that can be done by pharmaceutical companies to stop foreign nations from acting in their own self-interest, even when to do so hurts American consumers.[30] The most that could be expected, with little prospects of a positive return, is that the U.S., which is often regarded as a bully in international trade, will take up the cause. Yet that is most unlikely because one of the most common, albeit false, criticisms of the pharmaceutical industry is that it does *not* offer cut-rate prices on drugs to destitute third-world countries, especially for treatment of AIDS.

More generally, the higher prices in the U.S. also reflect a more robust demand for drugs in this country, which is related to the higher overall levels of income.[31] The issue of pricing is so complex that it becomes quite impossible to draw any negative inference from the change in overall price levels or the distribution in prices within or across countries, at least as long as we use the patent system.

Price Variations for Individual Drugs

A more telling objection, perhaps, is that some evidence suggests that the cost of particular drugs is rising in some instances more rapidly than inflation. For example, Public Citizen notes that the prices of particular drugs have risen by more than inflation—Acutane (22.7 percent), Oxycontin (15.4 percent), Glucophage (14.4 percent) and Allegra (10.9 percent).[32] But the presentation of isolated bits of information is not the same as a systematic examination of the available data. Here are some of the issues that have to be faced in dealing with the problem.

First, the rates that are quoted are average rates and thus do not take into account the price variation to different user classes, which are likely to be large given the institutional framework on which drugs are distributed in the U.S. In addition, the retail prices also reflect downstream price increments that are attributed to wholesalers, pharmacists and the prescription drug managers of various health plans over which the pharmaceutical houses exert little or no control. This problem, moreover, is not

confined to patented drugs, but also gives rise to risks in the generic sector, where once again hefty markups are always possible.

Second, it is unclear what inferences should be drawn from these increases. Some portions of the market basket will always increase more rapidly than the rate of inflation. It is important, therefore, to know the source of the increase. In these cases, there is no hint of collusion or other illegal activities that explains the price increases. Other possible explanations are multiple. A drug could have been perceived as risky at the time of launch, only to prove itself more successful over time. The higher level of safety commands a greater premium. Alternatively, the product in question could have proved its value in lower dosages or in combination with other drugs, which again increases its demand. Finally, the price increases could reflect changes in one portion of the overall market to the exclusion of changes in other portions of the market.

I list these possibilities not just as theoretical abstractions. Each of them has played its part in the recent furor over Abbott Laboratories' fourfold price increase of its popular AIDS drug Norvir, from $1.75 per day to $8.57 per day.[33] That increase provoked a strong outcry, which led to demands that Abbott be stripped of its exclusive rights to market Norvir under the so-called "march-in" rights under the Bayh-Dole legislation, which are triggered whenever a patentee fails to exploit its patented product in a "reasonable" fashion.[34]

It is important to know the source of the [price] increase.

But there is more to the story than that reported in the newspapers. First, the additional revenues were to be plowed back into further AIDS research. What fraction and for what projects is hard to say, but the larger point remains true. An increase in patent revenues during the life of a drug is an additional spur to the initial creation. It would be senseless as a matter of basic policy to insist that increases from initial prices should be prohibited or limited to the level of inflation. The net effect of that rule would be to induce drug companies to charge higher prices at the outset of drug treatment, thereby limiting early uses when the clinical effectiveness of a product is less well established.

As with any "ordinary" product, users are willing to pay higher prices when doubts about the drug's safety or efficacy have been removed through actual usage. The same process works in reverse; those drugs that have limited effectiveness or substantial side effects will see a reduction in market share and price. Price movements offer powerful signals of the worth of various goods and services that are every bit as useful for patented commodities as for any other goods.

Second, the price increase for Norvir did not cover all shipped units, owing to the pervasive forms of price discrimination, many of which are applauded. At the same time that Abbott raised its prices to the commercial sector, it guaranteed that free supplies would be provided for uninsured individuals, regardless of income. In addition, Abbott agreed to a permanent price freeze for sales to the two major programs available to AIDS patients. Both of these decisions may have been a self-interested effort to forestall a government response under Bayh-Dole, but if so, that is an argument against the aggressive reading of the statute that leads to choices that would not be made in an unregulated market. In any event, it certainly requires a downward recalibration of the stated price increases.

Third, the new uses of the drug give some explanation as to its repricing. When originally sold in 1996, Norvir was used in high dosages as a stand-alone drug, and was priced accordingly. Subsequently, research established that Norvir, when taken in conjunction with other AIDS drugs in small quantities, improves their effectiveness. In effect, the new use has made the drug more valuable in smaller dosages. A per unit price system ignores the positive synergetic effects from lower dosages, which should be reflected in market prices.

In light of these variations, it is no surprise that former Senator Birch Bayh testified that he did not think that the march-in rights under the basic statute were meant to usher in a de facto system of price controls, but should be reserved for (the thus far nonexistent) cases in which market forces were wholly ignored in the use and dissemination of government drugs.

The point is of special relevance because it turned out that the U.S. had contributed about $3 million, or roughly 1 percent of the cost, for the commercialization of the product, chiefly to sponsor some early clinical trials. The obvious point is that the entire public-private partnership under Bayh-Dole could not survive if that small hook is construed to authorize government control over pricing. Who would take a $3 million carrot that comes with a $1 billion stick? James Love, president of Essential Inventions, who is leading the charge for this novel exercise of march-in rights, insists that it is wrong to ask consumers to "pay twice" for Norvir, given that they had funded "the research" on the drug.[35] How easy it is to inflate

contributions: some research is not "the" research, and the novel invocation of Bayh-Dole would wreak havoc on the long-established patterns of funding research.

The Private-Public Interface

This last observation leads to the next question: why use the patent system at all when government research could sponsor the development of new drugs? This point, which Relman and Angell suggest but do not fully endorse, is of course subject to objections that bring us right back to the socialist calculation debate in the first half of the last century.[36]

As noted in dealing with the case of the bridge, a decision for government construction has at least two perils: The cost of construction could be higher owing to the inefficiency of government contracting, and the need for the bridge cannot be independently established by an appeal to private demand (which for these purposes is measured by the *maximum* amounts that all users are prepared to pay).

The same problems arise in the pharmaceutical industry. There is no doubt that the use of government funds to support basic research is an important component of any sensible system of drug production. But it is wrong to insist therefore that the process of commercialization of these basic patents should also be left in public hands once the basic science has been established by research that falls in the public domain.

The one solution that is bound to fail is that which seeks to place the full responsibility of commercialization in public hands.

There is within the patent literature endless debate over the question of whether a single firm with a monopoly position will do more to innovate on the patented invention than will a competitive industry in which no one enjoys a position of patent protection.[37] The issue is again hopelessly clouded at the theoretical level, because there are advantages each way.

The exclusive right means that the holder of the patent will spend lots of money for successful commercialization because it knows that it does not face competition. But that exclusive protection keeps out all sorts of other innovators unless they can negotiate deals with the patent holder, which can sometimes be done in licensing situations.[38] This ambiguity is not new, for in the 19th century there was much uncertainty as to whether any franchise given to build a bridge over public waters should be exclusive or nonexclusive, given the arguments that could be made both ways.[39]

Even today there is strong disagreement as to whether brokerage commissions should be exclusive or shared. And it is beyond doubt that Congress itself is somewhat leery of the public domain insofar as the Bayh-Dole Act takes affirmative steps to require government grantees to make good faith examinations of potential innovations to see if they are worthy of patents.[40]

The Failure of the Scientific Commons. Yet however close that debate turns out to be in principle, the one solution that is bound to fail is that which seeks to place the full responsibility of commercialization in public hands. Without some consideration of which projects will generate a market demand, the state will be as much at sea as it is in any other area where it purports to make social calculations without the benefit of price information.

The current system, by contrast, offers a more intelligent division of labor. There is a strong prohibition against the patenting of any natural substance on the grounds that these are most efficiently utilized when left in the public domain.[41] (Note that this rule is in contradistinction to a rule that allows for the patenting of a *process* to isolate and purify a natural substance.) Once that basic work has been done, any private firm can seek to develop a worthwhile marketable product based on it. That will still lead to patent races, but those races will take place over a shorter course, which means that the drugs in question can be developed in greater number at lower costs. In addition, the same basic research could lead to the development of two or more patented drugs that work in competition with each other, which allows for greater choice in responding to treatments.

"Me-Too" Drugs

Relman and Angell are skeptical about this last point as well, arguing that "me-too" drugs add nothing to the pharmacopeias and do little to reduce the prices of existing competitors.[42] But this position seems to be exceptionally shortsighted on both medical and economic grounds.

On the first, any "me-too" drug has to be sufficiently different from the original to be able to meet the standards for patent protection. Obvious extensions and imitations are denied patent protection under the law as it is, notwithstanding protestations from Relman and Angell to the contrary.[43] And those small differences could really make a difference in the grand scheme of things.

From the medical side, the availability of two drugs means that a second one could be tried if the first provides no additional benefit or has some adverse side effects. That me-too redundancy can prove vital, for example, when one drug within a larger family is recalled, because others will still be available. That happened when Merck announced on September 30, 2004, that it was recalling its COX-2 inhibitor Vioxx on the ground that its clinical use was associated with doubling of the risk of heart attack or stroke. The front page story showed that this was no small event, as Vioxx, which sold $2.5 billion, accounted for 11 percent of Merck's sales.[44] That day, the stock plunged over $12 per share, or 27 percent of share value, erasing some $26.8 billion in market capitalization.

There is some reason to ask whether this recall was the right decision, given the same base from which the doubling took place, and given the substantial benefits that Vioxx had in controlling ulcers. Indeed many physicians preferred it on that ground to Celebrex and Baxtra, its two Pfizer competitors. But for these purposes, the wisdom of the recall decision is not the prime concern. Rather, the key question to ask is what options would be available to the 84 million people around the world who have used the drug, and to others who might have used it in the future, if these two me-too substitutes had not been available. Here both Pfizer and independent experts have insisted that neither of its products have been associated with increased risk of stroke or heart attack. Clearly, even though all COX-2 inhibitors work in about the same way, the differences among them can prove critical in particular cases. Any strategy that looks down on me-too drugs undercuts the redundancy that proves so critical for containing adverse events.

Relman and Angell are engaging in a kind of industrial policy that hearkens back to the old socialist command and control economy.

From the economic side, the creation of a second drug means that the holder of the exclusive rights to market the first drug has lost its economic monopoly by the presence of a new competitor. Relman and Angell poohpooh this last possibility, claiming that they observe little or no price competition with the advent of me-too drugs. But, as noted above, while this may be true in the consumer market, it is not true in the managed care sector, where professional buyers are able to trade off the one drug against the other.

Dr. Thomas H. Lee supplies one useful illustration of the impact that a second product has on the first. He notes that the first-in-class of a new kind of cardiac stent produced a land-office business until a second form of cardiac stent came along to provide it with some competition.[45] It is, therefore, difficult to disagree with Lee's assessment that "[m]e-too products reflect and create competition among drug and device manufacturers, and that competition is also a powerful driver of better quality and lower cost."[46]

The point here has, if anything, deeper implications for industrial policy. In expressing their desire that drug companies go for new chemical entities that open up new vistas for treatment, Relman and Angell are engaging in a kind of industrial policy that hearkens back to the old socialist command and control economy. Sitting back in their armchairs, they think that we are all better off with high-risk/high-return investments than with low-risk/low-return investments.

They also are critical of the FDA for using a standard that compares a new treatment to a placebo and not to established drugs. All this is quite mistaken for there is no reason why they, or anyone else who sits on the sidelines, should have more information as to what strategy is better for what firm.[47] If it turns out that some company is prepared to market the fifth statin to lower cholesterol, it must believe that it can do something to persuade physicians and patients to leave their current product in exchange for a new one. In cases of "ordinary" markets, we welcome new entries as a way to expand consumer choice. There is no reason not to do the same here. The FDA should not be turned into an arbiter of marketability.

All this is not to say, however, that sound business acumen points inexorably to a strategy that favors "me-too" drugs. In principle, there is absolutely no reason to think that any uniform strategy will work for all market players, or even for all large pharmaceutical houses. In practice, it is possible to adopt any one of a countless number of research strategies, based on the knowledge of the strengths of one's own business and the apparent strategies of various competitors.

The Bain Study. In making this general declaration, nothing assures us that for-profit firms will adopt a winning strategy. Indeed, the recent and thorough Bain study on the entire industry castigates the large pharmaceutical houses for choosing the wrong strategies.[48] In the view of the Bain study, Big Pharma is too transfixed with mergers and too preoccupied with doing research across the board in the vain hope of discovering the next Lipitor

that will carry its profitability over the next generation. As jacks-of-all-trades and masters of none, they constantly lose out to smaller, more focused operations that have defined targets to which they can bring genuine expertise. The Bain study notes further that the rate of innovation in the small firms has been on average higher than those for larger firms.

One clear implication from this study is that Big Pharma should probably make deals with smaller producers who are proving themselves to be the more successful innovators, a practice that is becoming more common.[49] Perhaps this diagnosis better fits some firms than others. If so, we should expect some large firms to hire Bain as others spurn their advice. But for our purposes, the question is not whether this diagnosis is on the money (which I suspect that it is) but whether we think firms, commentators or legislators have the incentives to get to the bottom of the problem. The key point is that there is no reason to think that outsiders will do better on this question than insiders. Since we don't have problems of monopoly or collusion, it is best not to prescribe firm strategy.

It makes good sense from a social point of view to expend resources on advertising the benefits of the new treatment.

Yet rather than following the market test on this critical question, Relman and Angell march off in the wrong direction. While they do not call for the abolition of the patent system, they are obviously distressed with the current system of price variations, so their solution is to weaken drug patent protections.[50]

In their view, the way to measure the success of a large firm is to look at the percentage of its budget that is devoted to drug research as opposed to marketing and other activities. To be sure, this figure is far higher for pharmaceutical corporations than it is for most industries—about 18 percent to 4 percent, respectively. But these numbers should be understood as descriptions of how business is, or has been, done. In and of themselves they have no normative pop. No doubt that Relman and Angell, as good commissariats, would like to see that R&D percentage increased, especially at the expense of advertisement and marketing. But perhaps the opposite strategy would work better both for the firm and their customers. If large firms are not focused in their research, perhaps they should *reduce* the percentage of expenditures on research and specialize instead in "in-licensing," that is, licensing from smaller firms promising treatments that they have not developed.

This strategy, which seems to be on the rise, may well be a market response to the Bain criticism in that firms that have had mixed internal research results have decided to concentrate their efforts on other portions of the process of getting products from conception to the market. If so, we have seen a form of market specialization that at least holds out the possibility of some gains from trade. It is hardly the retreat from social responsibility that Relman and Angell make it out to be.

Marketing and Advertisement Practices

Relman and Angell's conviction that large pharmaceutical companies should have a commitment to do (as opposed to contract for) basic research leads them to condemn the industry's advertising and marketing practices. The marketing issues are viewed as efforts to woo the medical profession into abandoning their own independence and to persuade the public at large to either demand or purchase new high-priced drugs that are not worth their extra cost.

In responding to this impassioned criticism, it is important not to give a blanket endorsement to each and every pharmaceutical marketing practice that has ever been deployed. Puffery and temptation are risks in "ordinary" business, and they are risks in the pharmaceutical business as well. But once again the key question is one of measure and proportion, and on that score Relman and Angell overstate their case.

The Benefits of Advertising. The first point to note is that advertisements are not just a set of costs; they also provide a set of benefits that in some cases at least justify the associated costs. Here the relevant argument is not distinctive to the pharmaceutical industry, but applies across the board to any industry with high fixed and low variable costs. The key is to find ways to spread the cost of that first pill across as many users as feasible, for otherwise the product will not reach the market at all.

Thus, assume that we have a drug whose first pill costs $1 million to make, and each additional pill costs $2. The simple increase of one to two buyers cuts the cost per customer by almost half. Thus it makes eminently good sense from a social point of view to expend resources on advertising the benefits of the new treatment. If one thousand individuals use the pill, then the fixed costs are

reduced to $1,000 per person. If a million pills are sold, then those costs are at $1 per person, well within the range of the ordinary consumer.

But how do those other 999,999 individuals find out about the drug unless it is advertised? If, for example, it took $1.5 million to spread the word, the cost per customer drops sharply, for now the total expenditures of $3.5 million mean that the pill can cover its costs at roughly $3.50 per pill. The additional expenditures on advertising serve to lower the per-unit cost, increase the overall profit of the firm and offer benefits to individuals who would otherwise not know the drug was available.

What advertising does is allow the high-fixed costs of development to be amortized over a larger group of users. Once the additional advertising costs add more to the cost of medicine than they save through this amortization process, the ads will cease. This is not a situation in which there is a conflict of interest between the welfare of the firm and that of the public at large. Only if we ignore the gains from broader dissemination could we treat all advertising expenditures as a waste.

Relman and Angell spend little time on the basic economics of advertising and more on the endless efforts of "detail" men and women—the pharma sales force—to move new drugs at lavish conventions staged for physicians. But surely we should not dismiss these efforts as wholly useless. Moreover, the Bain study notes, "Physician details have become almost twice as expensive, evidenced by the drop in sales representatives' productivity of nearly 50 percent over the past seven to eight years."[51] Yet even this news is not an unalloyed good, because some advertising is necessary for needed therapeutics to reach their largest audience.

There is simply no reason to suppose that all the promotional efforts have no social benefits. The physicians who prescribe these drugs have their own reputations on the line and are themselves wary consumers of any and all products. The information that advertising provides could prove reliable in practice, and is in any event subject to contradiction or verification from neutral sources, as well as feedback from patients in individual cases. Feedback from bad reactions is often quick, so that systematic bad information is likely to be punished by disappointed physicians and hospitals.

In addition, the information supplied by detail men and women has to be put into context. No single firm has a monopoly on detailers, so physicians will also be in a position to hear the contrary point of view. Any balanced critique of these practices has to count their pluses as well. And while there are now extensive hospital and physician codes that limit access to detailers, it would be a mistake to assume that the health care industry would do better to ban their use. The dissemination of health care information is costly and tricky. It seems hard to believe that pharmaceutical companies should have no role in that process.

The Cost of Research

The analysis thus far has concentrated on how drugs are sold and the revenue that they produce. Of equal importance is the cost of new drug production. It is here that Relman and Angell take the position that the drug industry has inflated its estimates of the cost of production in a disingenuous effort to stave off the price-control measures that the authors think appropriate for this market. As Angell has written elsewhere, "Drug companies should be able to make a reasonable profit, but we need some system for curbing exorbitant prices that exploit Americans."[52]

The cost of new drug development must cover the costs of failed innovations.

Behind this view lies the belief that the costs of research and development of new drugs are not that high and represent a smaller fraction of the overall bill than the costs of advertising, to which they attach little benefit. Indeed, they take issue with the standard estimation of the cost of a new chemical entity of DiMasi, Hansen and Grabowski, which places that figure at around $800 million, preferring instead to adopt the estimate of $100 million made by Public Citizen.[53] They would surely be apoplectic at the figure announced in the Bain Study, which, based on more recent data, ups that number to about $1.7 billion.[54]

The root of the difficulty starts with a very simple question: what should be included in the cost of a new drug launch? Here everyone agrees that it covers the various efforts directed toward the discovery and synthesis of the new molecules, work that often takes years. In addition, there is the daunting array of preclinical and clinical trials, which are designed to deal with both the safety and efficacy of the drugs in question.

It is also clear that the costs of new drug development must cover the costs of failed innovations. As in the oil industry, the successful wells must produce enough revenues to cover the dry holes in order for any firm to remain in business. Looking just at the DiMasi study, it is easy to isolate the two sources of the sharp bump in cost

estimates. Bain reports that the costs of clinical trials, particularly at Phase II and Phase III, have gone up sharply, while the percentage of drugs that make it through trials to successful launch has dropped from about 14 percent to 8 percent from the 1995-2000 to the 2000-2002 period.[55]

The Bain data are by necessity somewhat limited, and the extrapolations from the DiMasi study may well be overstated, but those differences in estimation are not what accounts for the huge gulf between their work and the conclusions on which Relman and Angell rely. That difference kicks in at a much more fundamental level, stemming from the conviction that the proper mode for calculating drug costs should *not,* repeat *not,* include the cost of capital over time. Here it is critical to quote the key passage that critiques DiMasi for assigning a cost of capital of 9 percent per annum for each year between expenditure and realization:

> [T]he final estimate of the cost per drug is not the actual out-of-pocket cost, but what the authors [DiMasi et al.] call the "capitalized" cost—that is, it includes the estimated revenue that might have been generated over the long development period if the money spent on R&D had instead been invested in the equity market. This theoretically lost revenue is known as the "opportunity cost," and it is added to the industry's out-of-pocket costs of R&D. The authors seem to justify this interesting accounting maneuver on the grounds that from the perspective of investors, a pharmaceutical company is really just one kind of investment, which they chose among other possible investment options. But while this may be true for investors, surely it is not true for the pharmaceutical companies themselves. The latter have no choice but to spend money on R&D if they wish to be in the pharmaceutical business, so they have no "opportunity costs."[56]

[T]he signal that the costs of research and development are at political risk is sure to dull long-term innovations.

This passage only confirms the enormous gulf between economics and medicine, which reminds us today of the laments of the gap between "two cultures."[57] There is of course nothing unique about the pharmaceutical industry in this respect. One could say as well that no corporation faces opportunity costs because it could all go out of business, so that we should always ignore the first maxim of finance theory that all future cash flows should be discounted to present value.

But rather than recognize the manifest economic absurdity in denying the conventional wisdom, Relman and Angell cast digs at DiMasi and his colleagues, whose standard procedures are treated as some kind of parlor trick that eagle-eyed physicians are duty bound to unmask. After all, they tell us, no one can be confident of what takes place on Wall Street in light of recent events.

In this quixotic revisionist history of finance theory, they follow the lead of Public Citizen, which also believes that the only expenditures that matter are out-of-pocket expenses, and not the carrying costs of the deal.[58] The upshot is that half the costs of financing new drugs, which often take eight to 12 years to reach market, are treated as though they were not incurred at all. From that point it is easy to argue that other deductions from the ostensible cost figures should take place because, for example, expenditures in R&D are deductible. But the corresponding adjustment for aftertax income is not made as well.

All this is not to say that anyone can speak with confidence that DiMasi has the right numbers, or whether the higher Bain estimate will be confirmed when the recent data become more ample or are reviewed dispassionately by others. Nor is it to deny that the use of a single number to cover the widely disparate paths of new drug development may conceal as much as it reveals. But with that said, there is at least one simple test that says something about the overall state of health of the pharmaceutical industry today: Which way do the investment flows move?

If Relman and Angell are correct in their assertions, there is no reason why capital should not flow into pharmaceuticals, with stock prices trending sharply upward. After all, the costs are low, the marketing expenses are largely redundant and the prices are astronomical. But that pattern of robust growth is not what we see today.

New firms could avoid some of the problems that derive from the all-purpose research programs of the megafirm simply by building a better business model. Established firms can mend their ways or reinvent themselves, and may be doing that as we speak. But there are other problems that simply won't disappear that easily. The constant threat of price controls is dismissed by Relman and Angell on the grounds that so long as the profits of the industry exceed the costs of their R&D, there is nothing to worry about. "Prices," they assure us, "could be lowered substantially without coming close to threatening the R&D budgets of drug companies, much less their economic survival."[59]

But once again this statement bears no recognizable connection to any standard form of financial analysis. The simplest test of market value relies on some capitalized

value of the entire income stream. A firm that just covers its costs and no more will be worth zero. If a firm finds that the profits over its entire base of expenditures fall by one-half across the board, as a first approximation its capital value will fall by a like amount. And in this environment when the rate of return on new investments may be as low as 5 percent, if the Bain survey is to be believed, it is idle to assume that the position of firms will be improved by placing additional restrictions on how they conduct all aspects of their business. The claims that industry profits are exorbitant are fueled by this peculiar view of the accounting conventions that are needed to understand rates of return on multiyear investments. They show the serious danger in heeding the call for overall price controls. To be sure, in the short run, pharmaceuticals will continue to supply the market if they can cover their short-term costs. But the signal that the costs of research and development are at political risk is sure to dull long-term innovations. There are no free lunches here, any more than anywhere else.

Conclusion

At this point, there is little left to say except to insist that we go back to basics. Let analysis start off on the wrong foot and it will not right itself.

If the basic assumption of analysis is that the public loses whenever the firm gains, we should predict constant conflict and confusion in all sectors of private enterprise, including the pharmaceutical industry. But if we assume that firms generally have a good idea of what they are doing, and that voluntary transactions are win/win type situations, most of the critique of Relman and Angell is a form of intellectual huffing and puffing that addresses none of the serious questions of national policy toward business in general or the pharmaceutical industry in particular.

There is a larger lesson here: We shall never be able to get a sensible critique of the rights and wrongs in any particular instance if we keep kidding ourselves that "special" rules make the analysis of every industry *sui generis.* Whether we speak about rates of inflation, rates of innovation or rates of return, there are general principles available that allow for their systematic evaluation without indulging in the convenient if indefensible assumption that the usual rules of the game do not apply in the case at hand. The mistake of Relman and Angell is that they are so suspicious of the motives and actions of the pharmaceutical industry that they have not bothered to acquire the intellectual and technical tools that would permit an intelligent appraisal of the strengths and weaknesses of their favorite whipping boy. The global critics need to start over, from scratch.

Endnotes

1. Public Citizen, "America's Other Drug Problem: A Briefing Book on the Rx Drug Debate," Congress Watch, available at www.citizen.org/rxfacts [hereinafter Public Citizen], and Arnold S. Relman and Marcia Angell, "America's Other Drug Problem: How the Drug Industry Distorts Medicine and Politics," *The New Republic*, December 16, 2002 [hereinafter Relman and Angell].
2. *Congressional Daily*, March 11, 2004.
3. For discussion, see note 34.
4. See, for example, "Attacking High Drug Prices," *Chicago Tribune*, June 3, 2004, p. 22.
5. For an early statement of this view, see Oskar Lange and Fred M. Taylor, *On the Economic Theory of Socialism* (Minneapolis, Minn.: B.E. Lippincott, 1938); and H.D. Dickinson, *The Economics of Socialism* (London: Oxford University Press, 1939).
6. See Friedrich Hayek, "The Use of Knowledge in Society," *American Economic Review*, 35:519 (1945); and Friedrich Hayek, "Socialist Calculation: The Competitive 'Solution,'" *Economica, n.s.*, 8:125 *(1940).*
7. See Jacob Viner, "The Intellectual History of Laissez Faire," *Journal of Law and Economics*, 3:45 (1960). Viner writes: "I will carefully avoid using the term laissez faire to mean what only unscrupulous or ignorant opponents of it and never its exponents mean, namely, philosophical anarchism, or opposition to any governmental power or activity whatsoever."
8. See Richard A. Epstein, *Simple Rules for a Complex World* (Cambridge, Mass.: Harvard University Press, 1995), pp. 151-93.
9. *See* Richard A. Posner, "Natural Monopoly and Its Regulation," *Stanford Law Review*, 21:548 (1969).
10. For the most recent Supreme Court foray into this area, see *Duquesne Light Co. v. Barasch*, 488 U.S. 299 (1989). Note the different methods that have been tried to achieve the two goals of effective regulation: the elimination of monopoly profits without confiscating the capital investments made by the regulated industries.
11. One major example is in telecommunications, in which there was much effort to introduce competition to displace the statutory monopoly given to various local exchange carriers, or LECs. See, for example, *Verizon Communications v. Federal Communications Commission*, 535 U.S. 467 (2002); and *AT&T Corp. v. Iowa Utilities Board*, 525 U.S. 366 (1999). For discussion, see Douglas Lichtman and Randal C. Picker, "Entry Policy in Local Telecommunications: Iowa Utilities and Verizon, 2002," *Supreme Court Review* 41 (2003).
12. I address it in Richard A. Epstein, *Mortal Peril: Our Inalienable Right to Health Care?* (New York: Perseus Books, 1997).
13. See, e.g., Public Citizen.
14. Relman and Angell, p. 27.
15. For a recent elaboration of this theme, see Richard A. Epstein, *Free Markets Under Siege: Cartels, Politics, and Social Welfare* (London: Institute of Economic Affairs, 2004).
16. See, for example, the National Labor Relations Act of 1935.
17. For a defense of this proposition, see Frank H. Easterbrook and Daniel R. Fischel, *The Economic Structure of Corporate Law* (Cambridge, Mass.: Harvard University Press, 1991), pp. 1-40.
18. See Relman and Angell, p.27.
19. Bruce Kuhlik, general counsel for the Pharmaceutical Research and Manufacturers of America (PhRMA), and I have addressed some of these issues in Richard A. Epstein and Bruce N. Kuhlik, "Is There a Biomedical Anticommons?" *Regulation* 27: 54, 56-58 (Summer 2004). [hereinafter Epstein and Kuhlik].
20. For my development of this theme, see Epstein, *Mortal Peril: Our Inalienable Right to Health Care?* pp. 31-37.
21. Relman and Angell, p. 27.
22. See PhRMA, "Prescription Drug Price Trends are in Line with Medical Inflation," (Spring 2004), at www.phrma.org/publications/twopager/2004-04-29.986.pdf. The figures offered were designed to counter the charge that pharmaceutical companies

had systematically raised their prices in anticipation of the discounts that will be available under the Medicare Modernization Act, as of June 1, 2004. Enrollment in that program has in fact proved spotty in the early going.

23. Ibid.
24. See Joan Robinson, "A Fundamental Objection to Laissez-Faire," *The Economic Journal* 45:580 (1935).
25. See Ronald H. Coase, "The Marginal Cost Controversy," *Economica* (new series) 13:169 (1946).
26. See John F. Duffy, "The Marginal Cost Controversy in Intellectual Property," *University of Chicago Law Review* 71: 37 (2004) (updating the Coasean insight with regard to intellectual property).
27. For a clear discussion of these issues, see *Brand Name Prescription Drug Litigation*, 186 F.3d 781, 786-789 (7th Cir. 1999) (Posner, C.J.).
28. See, e.g., Public Citizen, Figure 1.D.1, p. 24.
29. For a brief discussion, see Epstein & Kuhlik, pp. 57-58.
30. It is important to be clear as to the source of the harm. It does not arise because an increase in prices in foreign markets will lead firms to reduce their price in the American market. No profit-maximizing firm would give up that advantage. Rather, the danger lies in the reduced rate of innovation stemming from the lower rate of anticipated return. The foreign nations capture all their gains from lower prices, and suffer only part of the losses from delayed innovation. Their position may be consistent with national welfare, but it is inconsistent with global social welfare.
31. See Patricia M. Danzon and Michael F. Furukawa, "Price and Availability of Pharmaceuticals: Evidence From Nine Countries," *Health Affairs* (October 29, 2003) (concluding that the differentials in drug prices across countries are roughly in line with income and smaller than the differences in the supply of other services).
32. Ibid.
33. For some relevant sources, see Bruce Japsen, "Abbott Defends Price Boost on AIDS drug at U.S. Hearing," *Chicago Tribune,* May 26, 2004, p. C1; "Abbott Laboratories Comments at NIH Public Meeting Regarding Norvir and Bayh-Dole March-in Provisions," PR Newswire, May 25, 2004; and Bruce Japsen, "Abbott AIDS Drug Pricing Leads to Review of Patent," *Chicago Tribune,* May 21, 2004, p. C1.
34. See Japsen, "Abbott AIDS Drug Pricing Leads to Review of Patent." The statutory text on which the argument is based is 35 USC § 203, which reads in relevant portion as follows:

    § 203. March-in rights

    (a) With respect to any subject invention in which a small business firm or nonprofit organization has acquired title under this chapter [35 USCS §§ 200 et seq.], the Federal agency under whose funding agreement the subject invention was made shall have the right, in accordance with such procedures as are provided in regulations promulgated hereunder to require the contractor, an assignee or exclusive licensee of a subject invention to grant a nonexclusive, partially exclusive, or exclusive license in any field of use to a responsible applicant or applicants, upon terms that are reasonable under the circumstances, and if the contractor, assignee or exclusive licensee refuses such request, to grant such a license itself, if the Federal agency determines that such

    (1) action is necessary because the contractor or assignee has not taken, or is not expected to take within a reasonable time, effective steps to achieve practical application of the subject invention in such field of use;

    (2) action is necessary to alleviate health or safety needs which are not reasonably satisfied by the contractor, assignee or their licensees;

    (3) action is necessary to meet requirements for public use specified by Federal regulations and such requirements are not reasonably satisfied by the contractor, assignee or licensees; or

    (4) action is necessary because the agreement required by section 204 has not been obtained or waived or because a licensee of the exclusive right to use or sell any subject invention in the United States is in breach of its agreement obtained pursuant to section 204.

    Standing alone, the text could be read as to make the possibility of government intervention a routine business, but in fact the interpretation of the statute has consistently gone the other way. See, e.g., Evelyn H. McConathy and Lisa Burgin Conte, "March-in Rights to Federally Funded Inventions," University Licensing, March 2002, p. 23, noting that the objective of the Act is commercialization, so that the United States "government is not anxious to exercise its march-in rights."
35. Ibid.
36. See Relman and Angell, pp. 30-32.
37. For the seminal paper on the question, see Edmund Kitch, "The Nature and Function of the Patent System," *Journal of Law & Economics* 20:265 (1977). For a modern reiteration of the problem, see John F. Duffy, "Rethinking the Prospect Theory of Patents," *University of Chicago Law Review* 71:439 (2004). For a more skeptical view, see Mark A. Lemley, "Ex Ante and Ex Post Justifications for Intellectual Property," *University of Chicago Law Review* 71:129 (2004).
38. For a discussion of these issues, see Richard A. Epstein, "Steady the Course: Property Rights in Genetic Material," in F. Scott Kleff, ed., *Perspectives on Properties of the Human Genome Project,* (San Diego, Calif.: Elsevier Academic Press, 2003), p. 159.
39. For the judicial decision that construed grants as nonexclusive when they were silent on the question, see *Charles River Bridge v. Warren Bridge,* 36 U.S. 420 (1837). The decision was by a 4 to 3 vote, with Story, J., in dissent. For a general history, see Stanley Kutler, *Privilege and Creative Destruction: The Charles River Bridge Case* (Baltimore, Md., and London: Johns Hopkins University Press, 1971).

40 35 U.S.C. §§ 200-211 (2000). Note that the commercialization rationale for the statute was explicitly endorsed by Joseph Allen, a former Bayh staff member: "What the public gets back is that these drugs will be commercialized." Japsen, "Abbott AIDS Drug Pricing Leads to Review of Patent."

41. See *Funk Brothers Seed Co. v. Kale Inoculant Co.*, 333 U.S. 127 (1948). For the limits, as applied to human-made bacteria, see *Diamond v. Chakrabarty*, 447 U.S. 303 (1980).
42. Relman and Angell, p. 32.
43. Ibid., p. 36.
44. For the front page stories, see Barbara Martinez, Anna Wilde Mathews, Joann S. Lublin, & Ron Winslow, "Merck Pulls Vioxx From Market After Link to Heart Problems", *The Wall Street Journal* , Oct. 1, 2004, at 1; Gina Kolata, "A Widely Used Arthritis Drug is Withdrawn", *New York Times*, October 1, 2004, at 1; Barry Meier, "For Merck, Defense of A Drug Crumbles at a Difficult Time", *New York Times*, October 1, 2004, C1 at C4.
45. Thomas H. Lee, "'Me-Too' Products - Friend or Foe?" *New England Journal of Medicine* 360:211 (Jan. 15, 2004).
46. Ibid., p. 211.
47. For one discussion of the decisions to invest in and price new pharmaceuticals, see Scott Hensley, "Biggest Drug Firm Faces Generics, But Has an Edge: Its Very Bigness," *The Wall Street Journal*, August 23, 2004, p. A1.
48. See Jim Gilbert, Preston Henske and Ashish Singh, "Rebuilding Big Pharma's Business Model," In Vivo: The Business & Medicine Report, Windhover Information, Inc., November 2003 [hereinafter Bain Study], 21:73.
49. See the discussion of the bidding contests for promising startups in Hensley, "Biggest Drug Firm Faces Generics, But Has an Edge: Its Very Bigness." *The Wall Street Journal*, August 23, 2004, p. A1.
50. Ibid.
51. Ibid.
52. Marcia Angell, "Importing Prescription Drugs from Canada," *Chicago Tribune*, August 20, 2004.
53. Joseph A. DiMasi, Ronald W. Hansen and Henry G. Grabowski, "The Price of Innovation: New Estimates of Drug Development Costs," *Journal of Health Economics* 22:151 (March 2003).
54. See Bain Study, Exhibit 1.
55. The usual protocol runs as follows. Phase I clinical trials are given to small numbers of individuals to determine the maximum levels of exposures that can be tolerated, taking into account adverse side effects. Phase II trials work off larger groups and experiment with different dosage levels to determine effectiveness. If a drug passes at this level, Phase III clinical trials are enormous undertakings, often on thousands of

patients, which are intended to make more definitive judgments about safety and effectiveness. The logistical elements here are formidable because if a new therapy promises a small improvement, it may have to be tested on huge populations. Ideally, these studies should be conducted in academic institutions where the controls are best, but the sheer size of the work requires that many different types of facilities be brought into the picture, creating higher costs and serious questions of quality control. For a brief account, see Relman and Angell, p. 28.

56. Ibid., p. 29.
57. See C.P. Snow, *The Two Cultures and the Scientific Revolution* (New York: Cambridge University Press, 1959). Snow referred to the gap between literature and physics from the standpoint of one who was extraordinarily proficient at both. He did not allude to the gap between medicine and finance, which years later looks every bit as large.
58. *"50 percent of the $802 million figure [of DiMasi] is theoretical:* Companies don't actually spend $802 million to discover and develop new drugs. That's because one-half of the $802 million figure represents the 'opportunity cost of capital.'" Public Citizen, p. 46.
59. Relman and Angell, p. 28.

About the Author

Richard A. Epstein is the James Parker Hall Distinguished Service Professor of Law at the University of Chicago. He is also the Peter and Kirstin Senior Fellow at the Hoover Institution. He has written numerous books and articles on a wide range of legal and interdisciplinary subjects. He has taught courses in civil procedure, communications, conflicts of laws, constitutional law, contracts, corporations, criminal law, jurisprudence, health law and policy, legal history, property, labor law, and workers' compensation.

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Direct all inquiries to: **Institute for Policy Innovation**
1660 S. Stemmons Freeway, Suite 475
Lewisville, TX 75067

(972) 874-5139 (Voice)
(972) 874-5144 (FAX)

Email: ipi@ipi.org
Internet Website: www.ipi.org