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Stagnation in the Drug Development Process:
Are Patents the Problem?

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Executive Summary

The poor performance of the pharmaceutical industry has become a major national concern in recent years, prompting major studies by both the Food and Drug Administration and Government Accountability Office. In spite of large increases in both private and public sector spending on biomedical research, the rate of new drug development has changed little.

The flip side of slow progress is higher costs. According to a series of studies by Tufts researcher Joe DiMasi, the cost of developing new drugs increased at a 10.9 percent annual rate over the years from 1987 to 2000 (7.4 percent after adjusting for inflation). This increase in costs is out of line with price trends in almost every other sector of the economy.

This paper examines how the incentives created by the current patent system of financing pharmaceutical research might be expected to produce this sort of cost explosion. Specifically, it considers the ways in which government patent monopolies distort incentives, so that pharmaceutical companies may not opt to minimize research costs. Since patent protection allows firms to sell drugs at prices that are several times their free market price, economic theory predicts that it will lead to a wide range of economic distortions, some of which affect research costs. The paper documents some of the perverse incentives created by patent monopolies in drugs.

It notes that:

- Pharmaceutical companies can use their research spending as a way to punish countries that impose price controls on their drugs and reward countries that allow them unfettered patent monopolies. The industry has claimed that this is the reason they have relocated research from Europe to the United States. It also is the reason that they claim they have not relocated research to developing countries where costs are lower. The profits that the industry receives by pressuring governments to raise drug prices would likely dwarf any savings from moving to countries where research costs are lower.

- The existence of patent monopolies means that pharmaceutical companies stand to gain large profits by currying the favor of key politicians. For example, if the government mandates that programs such as Medicaid pay for a specific drug, the potential profits can be enormous. (By contrast, if drugs were sold in a competitive market, in the same way as pens, a government mandate for increased spending on pens has limited effect on the profit of any specific pen manufacturer.) This fact could lead a pharmaceutical manufacturer to locate, or keep, research facilities in the district of powerful members of Congress, even if lower cost locations exist.

- Since the length and scope of patent protection is determined through the political process, the pharmaceutical industry can substantially increase its profits by getting political support for stronger protection. Payments to researchers, especially university-based researchers, can be an important way to gain support for stronger patent protections. In effect, research payments to universities are a way to share monopoly patent rents. The pharmaceutical industry can use this money to get prestigious and powerful educational institutions to join them in lobbying for stronger patent protections.

- Another major component of research costs are the payments that the industry makes to doctors for participating in clinical trials. Since the industry is dependent on the prescribing habits of doctors for their profits, it is very important for them to enjoy their goodwill. Excessive payments to doctors for their participation in clinical trials can be a mechanism of effectively providing a kickback to doctors who prescribe their drugs. For this reason, firms would have little incentive to minimize their payments for participating in clinical trials.

Since the issues described in this paper involve practices that are at least unethical, if not actually illegal, there is no publicly available data that can allow their impact to be readily quantified. However, economic theory predicts that there will be some amount of added cost due to these factors and a large body of anecdotal evidence suggests that the additional costs could be substantial. In other words, it is plausible that the cost of developing new drugs has been rising rapidly, not because of the inherent difficulties of the research process, but rather because of the perverse incentives created by the patent system.

Introduction

The rate of development of new drugs has changed little over the last decade, in spite of the fact that real spending on bio-medical research in both the private and public sectors has more than doubled. Furthermore, the vast majority of new drugs that are approved by the Food and Drug Administration (FDA) largely replicate the function of existing drugs, rather than constituting important medical breakthroughs. This stagnation has been a topic of major concern, prompting recent studies by both the Food and Drug Administration (FDA) and the Government Accounting Office (GAO).[1]

These studies examined a variety of factors that may play a role in impeding the progress of research in the pharmaceutical sector, including patent rules. Both studies identified ways in which the perverse incentives created by patents may obstruct the progress of research. For example, the GAO study highlighted the fact that much research is diverted towards developing copycat drugs, since this may be a much easier route to earning patent rents than developing a breakthrough drug that provides a qualitative improvement over existing drugs. However, the distortions created by patent protection actually go far beyond the issues identified in these studies. This paper outlines additional mechanisms through which patent protection can be expected to raise research costs and slow progress.

[1] FDA 2004, GAO 2006.

The Basic Problem: Slow Progress and Higher Costs

The pharmaceutical industry reports that its spending on research and development more than doubled from $15.7 billion in 1993 to $38.8 billion in 2004 (in 2004 dollars).[2] Over the same period, funding for the National Institutes of Health also doubled, rising from $13.3 billion to $28.0 billion (in 2004 dollars).[3]

However, there was little apparent gain from this increase in private and public spending in the number of new drugs approved. In the years 1991-1993, the FDA approved an average of 75 new drugs a year. In the years 2002-2004, the average number of new drugs approved each year had risen by just 17 percent to 88 per year. Furthermore, the average number of approvals that were rated as "priority" reviews, meaning that they constituted qualitatively new treatments, had actually fallen slightly, from 18 per year in the 1991-1993 period to 17 per year in the 2002-2004 period. The number of priority reviews that involved new molecular entities had also fallen, from 13 in the earlier period to 11 in the most recent period.[4] In short, there is little evidence that the large increases in private and public expenditures on biomedical research had any dividend in terms of the quantity or quality of drugs being developed by the pharmaceutical industry.

The flip side of rising expenditures producing few dividends in the form of new drugs is the rising cost of drug research. A set of studies by Tufts economist Joe DiMasi shows that research costs have risen at an annual rate of 10.9 percent between 1987 and 2000 (7.4 percent in real terms).[5]A recent Commerce Department study projected this growth rate forward to 2005, and concluded that the cost of researching a new drug has increased by 540 percent from 1987 to 2005.[6] It is important to note that DiMasi's estimates only refer to the private research costs incurred by the pharmaceutical industry. The estimates do not include expenditures by National Institutes of Health for basic scientific research that plays a crucial role in developing new drugs.

It is striking how inconsistent the rise in the cost of developing new drugs is with other price trends in the U.S. economy. Few other items have risen nearly as rapidly as the cost of researching new drugs. For example, if the price of a gallon of milk had risen as rapidly as the cost of developing new drugs, milk would have been selling for $14.60 per gallon in 2005.

If the price of a coast-to-coast airline ticket had risen as rapidly as the price of developing new drugs, it would cost more than $3,000 to fly from New York to Los Angeles in 2005, as shown in Figure 1. If the price of desktop computers had followed the same path as the cost of developing new drugs, a standard desktop computer that cost $2,500 in 1987 would sell for more than $16,000 today. Instead, consumers can buy a computer in 2007 for less than $500 that is far better than any desktop computer available in 1987. Consumers have clearly benefited from the fact that the price of most items has not followed the same path as the cost of prescription drug research.

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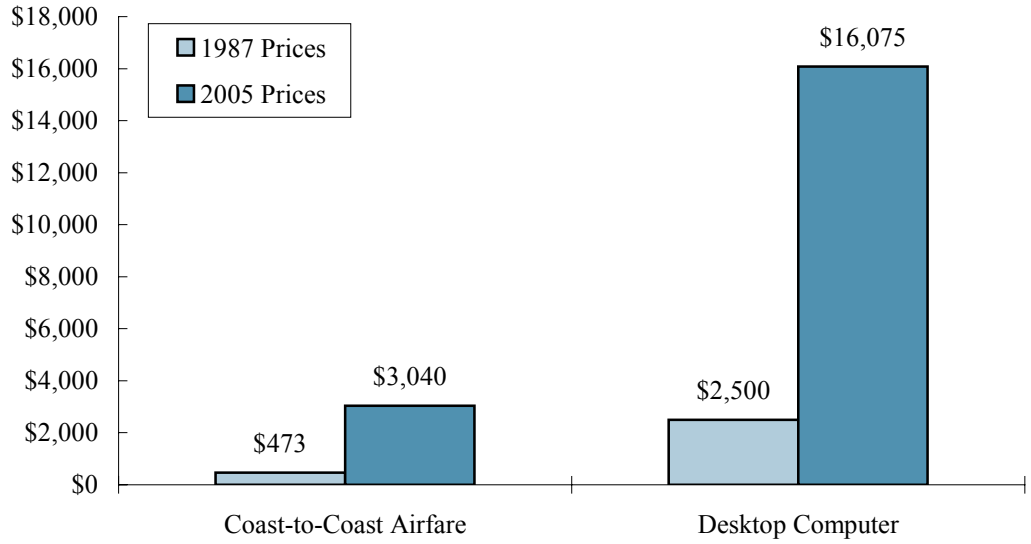
[2] PhRMA 2005.
[3] NIH 2006.
[4] These numbers are taken from FDA 2006.
[5] DiMasi et Al. 1999 and 2003.
[6] USDOC 2005.

Figure 1: If Other Prices Had Risen as Much as the Price of Drug Research



Source: Author's calculations.[7]

The explanations for the sharp divergence in the cost of developing new drugs from other prices in the economy take two different directions. One of these approaches seeks to explain the sharp rise in the cost of developing new drugs by factors intrinsic to the bio-medical research process. The logic of these arguments depends on the claim that, as medical science develops, it becomes more difficult to make new breakthroughs. In this view, scientists have already grabbed the low-hanging fruit, so that future innovations will be much harder to achieve.[8] While this could be true, there is no obvious reason that progress in medicine should be slowing at a time when progress in other areas, like computer science, is accelerating. It is also worth noting that the cost of many research tools is plummeting due to the enormous growth in computer power.

The other main line of explanation for the sharp rise in the cost of developing new drugs places the blame on the distortions created by patent monopolies. Like any form of government intervention in the market, patents create a variety of perverse incentives. These incentives can lead research dollars to be misdirected and create waste in the research process. This paper discusses some of the ways in which the incentives created by patents can add to the cost of developing new drugs.

[7] The 1987 prices were advertised prices from various publications. The 2005 price assumes the annual 10.9 percent rate of increase in the cost of drug research found by Dimasi et Al. 2003.

[8] GAO 2006: pp 25-27.

The Economics of Patent-Supported Research Spending

The system of patent-financed research creates a fundamentally different set of incentives for pharmaceutical companies than exists for firms that operate without this sort of government intervention. Drug companies maximize their profits by finding ways to maximize the value of their patent monopolies, by increasing the length or strictness of patent protection or getting more buyers at patent-protected prices. This can lead drug companies to deliberately take steps that increase research costs, because the costs are more than offset by the greater revenues they earn from their patent monopolies.

If the sale price of patent-protected drugs is sufficiently high relative to their marginal cost of production, then even a small increase in sales could result in profits that would swamp any additional research expenditures. Generic drugs sell on average for just 29.3 percent of the price of patent-protected drugs.[9] In principle, there is no reason to believe that brand drugs would be any more expensive to produce than generics, therefore the difference between the sale price of brand drugs and generic drugs is the extra profit margin that is allowed as a result of patent monopolies. In other words, more than 70 percent of the sale price of a typical brand drug is attributable not to production and distribution costs, but rather the markup the company can command because of patent protection.[10]

According to the industry's estimates, research costs are equal to approximately 17 percent of total sales. Given these ratios, the additional patent rents that would result from even a small increase in sales can offset a very large percentage increase in research costs. For example, the additional patent rents associated with a 5 percent increase in drug sales (0.05*70 percent = 3.5 percent of total current sales) would more than offset additional expenditures that raised the cost of research by 20 percent (0.2 * 0.17 percent = 3.4 percent of total current sales). For this reason, it is likely that there are many occasions in which drug companies may not maximize profits by minimizing research costs.

There are an endless number of ways in which efforts to maximize profits from patent monopolies can inflate research costs, but this paper will focus on three.

1. The use of political, rather than economic considerations, in the location of research facilities;

2. Excessive payments to researchers as a way to gain political allies; and

3. Excessive payments to doctors conducting clinical trials as a way to encourage them to write prescriptions.

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[9] This figure is calculated based on data from the National Association of Chain Drug Stores, cited in United States Census Bureau 2007.

[10] This 70 percent is likely to understate the extent to which the price of brand drugs is increased as a result of patent protection. Some generic drugs will be sold for prices that are higher than the competitive market price because generic manufacturers get 6 months of exclusivity if they are the first generic to enter the market. In the same vein, some brand drugs will be competing against generics because their period of patent protection has already expired.

Given the incentive structure created by drug patents, profit maximizing firms will engage in all three of these practices to some extent. Since these practices are at least unethical, if not actually illegal, there is no publicly available data that would make it possible to determine how important each factor has been in driving up research costs. However, explicitly recognizing these distortions may facilitate the development of methodologies that would allow their impact on research costs to be better measured.

Locating Research to Maximize Political Influence

If the pharmaceutical industry operated like most other industries, the main consideration in locating production facilities would be minimizing costs. However, the location of a research lab can be an important bargaining chip with a government over its pharmaceutical pricing policies. The United States is the only wealthy country that grants drug companies unrestricted patent monopolies. Other wealthy countries negotiate drug prices or impose price controls to limit the extent to which drug companies exploit their patent monopolies. As a way of influencing government drug pricing policies, pharmaceutical companies can promise to locate labs in countries that have more generous pricing policies, or move them away from countries with less generous policies, even if this decision leads to higher costs.

In fact, this seems to be exactly what at least one top executive in the industry effectively claims the industry does. Sidney Taurel, the President and Chief Executive Office of Eli Lilly, recently gave a speech in which he claimed that pharmaceutical companies had relocated their research operations from Europe to the United States because of the price controls and/or negotiated prices that the industry faces in Europe.[11]

It is important to realize that under TRIPS, and other international treaties, companies are guaranteed that they will get the same patent protection for their innovations regardless of where they choose to locate their research. This means that the stringency of a country's patent laws or its policies on controlling price controls are exactly the same whether the patent in question is based on research performed in the United States, Europe, or the developing world.

Effectively, Mr. Taurel was saying that even though it may have been cheaper to carry on research in Germany or France, pharmaceutical companies have shifted operations away from these countries because their governments restricted drug prices. Presumably, Mr. Taurel hoped this example would scare his audiences about the prospect of implementing price controls, or in other ways restricting drug prices in the United States.

If the relocation of research, or the threat to do so, can affect drug pricing policies in Europe or the United States, then it may be profit maximizing for drug companies to pay more money for their research than necessary, since the companies will be more than compensated for any additional research expense by getting higher prices for their drugs. This effort at extracting concessions on drug pricing policies appears to be behind the industry's reluctance to locate research in developing countries like India, Thailand, and Brazil, which have large pools of highly skilled scientists who receive a fraction of the compensation of their counterparts in the United States.

Other industries, like the software industry, have achieved considerable cost-savings by taking advantage of the rapid growth in the supply of highly skilled workers in the developing world. However, the pharmaceutical industry appears to be more interested in increasing the price of its drugs in developing countries, by pressuring governments to impose stronger patent protection,

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[11] Taurel 2003. Other industry representatives have also claimed that Europe's policies on drug pricing were an important factor in the decision to relocate research spending to the United States (e.g. Cowell 2003 and Harris 2003).

than in minimizing its research costs. The potential gain from higher drug prices in these countries is likely to dwarf any savings from lower cost research.

There are other ways in which the pharmaceutical industry may be able to increase its monopoly profits by paying more than necessary for prescription drug research. For example, it may prove useful to locate research in the districts or states with powerful members of Congress even if these districts are not the lowest cost place to carry out research. The payoff from such decisions in higher drug prices and sales could dwarf any increase in research costs from such decisions.

For example, according to a 2005 *Washington Post* article, Eli Lilly and Company benefited from a clause inserted into a large budget bill that required state Medicaid programs to pay for an anti-depressant drug that it manufactured rather than a much cheaper generic alternative.[12] The congressman who represents a district near where Lilly's headquarters is located was able to use his position as a member of the House Energy and Commerce Committee to get the clause inserted. The article reported that this clause would increase Lilly's sales by several hundred million dollars over the five year period covered by the bill. In this case, Lilly received a very substantial return as a result of locating in a district with a powerful member of Congress. The additional profits that it is likely to earn from having this provision included in the budget bill would almost certainly be far larger than any potential savings on research costs that might result from moving its research to a lower cost area or country.

The potential gains from getting or keeping the favor of powerful members of Congress are likely to far exceed any savings from moving to locations with lower research costs. Given the enormous patent rents that the drug industry is able to extract, even a relatively small increase in patent rents is likely to dwarf any potential savings in research costs. As a result, profit maximizing pharmaceutical companies are likely to place far more emphasis on locating research in areas/countries where it will have the most political impact, rather than in areas where the research costs will be lowest.

[12] Weisman 2005.

University-Based Research: Buying Friends in the Ivory Tower?

Another important way in which the drug industry's research decisions can affect its ability to gain monopoly rents is by winning important political allies who will support laws providing for stronger patent protection. The obvious example would be providing research funding to university-based researchers. This money has won the industry the support of many powerful universities in arguing for strong patent protection, since these institutions now have a direct stake in these laws. In addition to the lobbying capabilities of these universities, the industry also benefits from the legitimacy conferred on their efforts by non-profit institutions that ostensibly exist to promote the advancement of knowledge.

For example, in 2004, the Association of University Technology Managers (AUTM) wrote a statement formally opposing efforts to force the National Institutes of Health (NIH) to use its "march-in" rights to require that compulsory licenses be issues for two drugs (Ritonavir and Latanoprost) developed with a substantial amount of NIH support.[13] More recently, AUTM took a strong position opposing the creation of an explicit research and experimentation exception in U.S. patent law.[14] There are numerous other instances in which individual universities or groups of universities have taken public positions or even entered lawsuits on the side of the pharmaceutical industry. From a public relations standpoint, the voice of non-profit institutions can be extremely valuable in advancing the position of the pharmaceutical industry.

For this reason, the pharmaceutical industry, an industry that already spends hundreds of millions of dollars each year on lobbying and public relations, may reasonably view research expenditures at universities as part of an effort to gain public support and political power to allow them to maximize their patent rents. In effect, the payments that the pharmaceutical industry makes to university-based researchers (a portion of which generally goes directly to the university to cover operating expenses) should be viewed as not only research costs, but also as payments for goodwill and political influence. Therefore, it could often be profit maximizing for the industry to make expenditures for university-based research that are considerably higher than what may actually be necessary to pay for the research. This would ensure that the universities get a substantial portion of the patent rents, and therefore have an incentive to publicly campaign for more stringent patent protection.

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[13] AUTM 2004.
[14] AUTM 2005.

Payments for Clinical Trials: A Legal Form of Kickbacks?

Finally, the process of clinical testing is not only an opportunity to determine the effectiveness of new drugs; it is also an opportunity to gain the goodwill of the doctors who are responsible for the decisions about which drugs to prescribe for patients. Here also, the industry may have little incentive to minimize costs. If a drug company pays doctors more than is necessary to take part in clinical trials, it may recoup the additional expense many times over in the increased sale of its drugs as a result of additional prescriptions for its drugs written by these doctors. In effect, the excess fees for drug trials are a way for the industry to provide kickbacks to doctors.

There have been numerous news reports in recent years of what appear to be excessive payments to doctors for taking part in clinical trials.[15] Given the incentives created by patent monopolies, and the difficulty that government regulators face in trying to supervise the conduct of drug companies and doctors, it is virtually inevitable that some drug companies will use payments for clinical trials as a mechanism to get doctors to look favorably on their drugs.

The desire to cultivate doctors as clients may also explain the reluctance of the pharmaceutical industry to shift clinical trials to countries where they can be conducted at lower costs. The U.S. market accounts for close to 50 percent of the industry's world-wide sales, and because of its high prices, far more than half of its profits. Furthermore, doctors have far more freedom in prescribing decisions in the United States than in other countries. For all of these reasons, it may be profit maximizing for firms to pay higher fees than necessary to carry through its clinical trials since they will be more than compensated with increased drug sales at patent monopoly prices.

[15] For example, see Eichenwald and Colata 1999a, Eichenwald and Colata 1999b, and Harris 2004.

Patent Monopolies: Incentives for Waste or Incentives to Innovate?

Patent monopolies are a very crude governmental mechanism for supporting innovation, especially in an industry where there are important asymmetries of information and third party payers, like the prescription drug industry. The paper has outlined three ways in which there is reason to believe that research expenditures by the pharmaceutical industry may be higher than necessary, because the drug companies use their research spending as a way of maximizing patent rents.

There are no easy methods for quantifying the waste that results from these factors both because the pharmaceutical industry is not likely to be forthcoming about practices that are unethical, if not actually illegal, and because it would be arduous to develop independent assessments of relative costs. For example, in principle, it should be possible to estimate the cost of carrying out research in India or other developing countries with substantial expertise in drug development, but there is no easy way to measure the relative quality of the resulting research. Without such a measure, it is not possible to determine the extent to which drug manufacturers may be willing to pay more to carry through research in the United States because they are actually hiring better researchers, as opposed to the possibility that they are simply rewarding the country for its strong patent protection and absence of price controls.

The same problem would arise with efforts to quantify the other sources of waste identified in this discussion: excess payments to university-based researchers and excess payments to doctors conducting clinical trials. In both cases, there are important quality factors that cannot be readily measured. In time, if the research process become more diffuse so that more bio-medical research actually takes place in developing countries, and data on the cost of this research is accessible to the public, then there will be a better basis to assess the extent to which efforts to exploit patent monopolies may be increasing the cost of the pharmaceutical industry's research.

Of course, there are many other sources of waste induced by the patent system, both in the research process and in the distribution of drugs. The patent system can provide large incentives to develop copycat drugs of little therapeutic value, since the return on such drugs can quite possibly be larger than developing breakthrough drugs. According to the FDA, close to 70 percent of the drugs it approves fall into the "standard" category, which means that they do not represent qualitative breakthroughs over existing drugs.[16]

Not only is it wasteful to devote such a disproportionate share of research spending on drugs that largely duplicate the purpose of existing drugs, it also might lead to an inflation in the cost of researching each drug. The FDA is likely to demand a higher standard of proof for the safety and efficacy of a drug that is considered duplicative of existing drugs than a breakthrough drug that is a qualitative advancement in treatment.

An examination of the average size of clinical trials for FDA-approved labels between 2000 and 2002 found that the average trial size for drugs subject to priority reviews was 1,461, while the average trial size for drugs subject to standard reviews was 2,667, more than 80 percent larger.[17] In

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[16] The breakdown of drug ratings can be found at FDA 2006.

[17] Love 2003, Table 4.0-2. DiMasi, et al. 2003 reached the opposite conclusion in an assessment of clinical trial sizes based on proprietary information from several large pharmaceutical manufacturers.

this way, the perverse incentives created by the patent system not only lead pharmaceutical companies to research drugs that might serve little purpose in the absence of patent protection, they might *raise* the average cost of researching new drugs, since duplicative drugs may require more testing for approval than breakthrough drugs.

The patent system also provides incentives for secrecy, since a pharmaceutical company will want to keep control over all of its findings until it believes that it has obtained intellectual property rights to any discoveries that have marketable value. In addition to reducing efficiency across the industry, this secrecy can be dangerous for consumers, since the patent system creates incentives to conceal or even falsify research findings that reflect poorly on a company's drugs. In principle, the threat of legal sanctions should discourage such practices, but the frequency with which they become public suggests that many drug companies are prepared to risk the consequences of being caught.

Conclusion

The pharmaceutical industry has justified the large mark-up on their drugs as being necessary to recover their investment in researching and developing new drugs. According to the leading researcher on this topic, the cost of developing new drugs has been rising at an average real rate of more than 7 percent since 1987.

However, economic theory and a considerable amount of evidence suggest that the industry's research costs may be substantially inflated, because they include spending that has the purpose of increasing patent rents, rather than just carrying through research. This paper has identified three ways in which research spending could be inflated:

1. Locating research to maximize political influence, rather than minimize cost;

2. Making excessive payments to university-based researchers for their support in political battles over patent rights; and

3. Making excessive payments to doctors for conducting clinical trials as a way of rewarding them for prescribing more of the company's drugs.

Economic theory predicts that all of these practices occur to at least some extent. More evidence is necessary to determine how important these factors have been in driving up the cost of researching drugs over the last two decades.

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