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Patents and New Product Development in the Pharmaceutical and Biotechnology Industries

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This paper examines the rationale for intellectual property protection in the development of new pharmaceutical products. Prior survey studies of R&D executives have found that patents play a more critical role in appropriating the benefits of innovation in pharmaceuticals compared to other high tech industries. This paper considers why this is so, based on an analysis of the economic characteristics of R&D costs and returns in the pharmaceutical and biotechnology industries. The final section examines recent policy developments and issues surrounding patent lifetime and generic competition in this industry.

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INTRODUCTION

Grilliches, in a 1992 survey paper, found that high social returns to research and development (R&D) are a major factor underlying the growth in per capita income and consumer welfare during the 20th Century (Grilliches 1992). Many of the studies done by economists on this topic have found that the social returns to R&D are more than twice the private returns. A primary reason for this finding is that positive externalities are generally associated with industrial innovations. As F.M. Scherer stated in his leading graduate text in industrial organization, "Making the best use of resources at any time is important. But in the long run it is dynamic performance that counts." (Scherer 1980, p. 407)

The pharmaceutical and biotechnology industries, which are among the most research-intensive industries, have been the focus of several studies on cost-benefit and social return on R&D studies. Cutler and Mcclellan (2001) surveyed a number of studies that investigate the impact of new drugs on increased longevity, worker productivity, and savings in other types of medical expenditures. They find significant aggregate net benefits to society from new drug introductions.
Their analysis is consistent with many cost-benefit analyses targeted toward specific medical conditions such as cardiovascular disease, depression, and infectious disease. These studies have also found high incremental social benefits from new drug innovation.1

Another general finding of the academic literature is that public policy actions can have a significant influence on the rate of innovation in particular industries. Among the key industrial policies influencing the innovative process in pharmaceuticals are the public support of biomedical research, patents, Food and Drug Administration regulatory policy, and government reimbursement controls (Towse 1995). The focus of this paper is the role and impact of patents and intellectual property protection in the discovery and development of new pharmaceutical and biotechnical products.

The importance of patents to pharmaceutical innovation has been reported in several cross-industry studies. Richard Levin et al. (1987) and Wes Cohen et al. (1997), have undertaken surveys of U.S. R&D managers, in a large cross-section of industries, to identify the most important and necessary factors in appropriating the benefits from innovations. These factors included the competitive advantages of being first in the market, superior sales and service efforts, the secrecy and complexity of productions and product technology, as well as patents. Both studies found that the pharmaceutical industry placed the highest importance on patents. By contrast, many other research-intensive industries, such as computer technologies, scientific instruments, and semiconductors, placed greater stress on factors like lead-time and “learning by doing” efficiencies in production accruing to first movers. This reflects the fact that R&D investment periods and product life cycles are typically much shorter in these industries. Furthermore, their new products often involve complex systems of many components as opposed to the discrete nature of new chemical and biological entities. As a consequence, the costs of imitation relative to the costs of innovation are much higher in many other high-tech industries compared to pharmaceuticals.

The findings of these studies are in accordance with an earlier study performed by the British economists Taylor and Silberston (1973). Based on a survey of R&D managers in the UK, they estimated that pharmaceutical R&D expenditures would be reduced by 64 percent in the absence of patent protections. By contrast, the corresponding reduction was only 8 percent across all industries. Similar findings were reported by Edwin Mansfield, in a survey of the research directors of 100 U.S. corporations.2

Some individuals have called for the abolishment of pharmaceutical patents on the grounds that they give rise to excessive profits and high prices on new medicines (Baker 2003). However, the suggestion that the government could replace the $27 billion dollar R&D effort of the private pharmaceutical industry, and produce an equivalent stream of new pharmaceutical products, is highly problematic on both economic and public policy grounds. Opponents of drug patents also ignore the fact that new products lead to social welfare gains for consumers, even when supplied by a single
firm under a patent exclusivity grant. In addition, price competition occurs in the pharmaceuticals market under the current system when closely substitutable medicines in the same therapeutic family are introduced. Finally, there is intensive price competition when the originating brand’s patents expire and generic entry occurs.

The following sections of this paper examine the economic characteristics of the R&D process in pharmaceuticals that make patents so critical. Sections II through IV discuss the costs of innovation in pharmaceuticals and the effects on innovative and imitative competition of the 1984 Hatch-Waxman Act. Section V considers whether the biotech industry is different from the pharmaceutical industry in terms of R&D costs. Section VI considers the distribution of returns on R&D in these industries. The final section presents conclusions and policy considerations.

R&D Costs for a New Drug

Introduction

The explanation for why patents are more important to pharmaceutical firms in appropriating the benefits from innovation follows directly from the characteristics of the pharmaceutical R&D process. It takes several hundred million dollars to discover, develop and gain regulatory approval for a new medicine. Absent patent protection, or some equivalent barrier, imitators could "free ride" on the innovator's FDA approval and duplicate the compound for a small fraction of the originator's costs. Imitation costs in pharmaceuticals are extremely low relative to the innovator’s costs for discovering and developing a new compound.

One of the reasons why R&D is so costly in pharmaceuticals is that most new drug candidates fail to reach the market. Failure can result from toxicity, carcinogenicity, manufacturing difficulties, inconvenient dosing characteristics, inadequate efficacy, economic and competitive factors, and various other problems. Furthermore, the full R&D process from synthesis to FDA approval involves undertaking successive trials of increasing size and complexity. Typically, many thousands of compounds are examined in the pre-clinical period for every one that makes it into human testing. Only 20 percent of the compounds entering clinical trials survive the development process and gain FDA approval (DiMasi 1995). The pre-clinical and clinical testing phases generally take more than a decade to complete (Kaitin and DiMasi 2000).

In a recently completed study, DiMasi et al. (2003) have examined the average R&D cost for drugs introduced into the market in the late 1990s. Data were collected on R&D costs for a randomly selected sample of 68 investigational drugs from 10 multinational firms. DiMasi, et al. found that the representative new product approval incurred out-of-pocket costs of over $400 million. This includes money spent in the discovery, pre-clinical and clinical phases as well as an allocation for the cost of failures.

Figure 1 shows a breakdown of total R&D costs per approved drug incurred during the pre-clinical and clinical R&D phases. Expenditures in the clinical period account for roughly 70 percent of total out-of-pocket expenditures. This reflects the fact that clinical trials are very expensive on a
per patient basis; many drugs must be tested for every one approved, and drugs that do make it to the final testing phase and FDA submission typically require pre-market testing on thousands of patients.

Figure 1 also shows R&D costs capitalized to the date of marketing at a representative cost of capital for the pharmaceutical industry of 11 percent. The average capitalized R&D cost for a new drug introduction during this period is $802 million, or nearly double the out-of-pocket expenditure. Capital costs are high in this situation because of the long time periods involved in pharmaceutical R&D. More than a decade typically elapses between initial drug synthesis and final FDA approval. Since pre-clinical expenditures occur several years prior to FDA approval, these costs are subject to greater compounding at the industry cost of capital of 11 percent. Therefore, they account for a greater proportion of total capitalized cost compared to total out-of-pocket costs (42 percent versus 30 percent).

R&D costs per new drug approval in the 1990s increased at an annual rate
of 7.4 percent above general inflation when compared to the costs of the 1980s approvals. Major factors driving this increase are the complexity and number of clinical trials, which have increased significantly in the 1990s compared to the 1980s. One important factor underlying this trend is the pharmaceutical industry’s increased focus on chronic and degenerative diseases; such conditions require larger trial sizes to establish efficacy and longer time periods for observation.

A number of factors could alter the growth pattern for future R&D costs. Emergent technologies may have profound effects on R&D productivity in the next decade. The mapping of the genome, and related advances in fields like proteomics and bioinformatics, has led to an abundance of new disease targets. Some industry analysts have hypothesized that these developments may actually cause R&D costs to rise in the short run (Lehman Brothers 2001). The basic reason is that these new technologies require substantial investments up front, and to date they have generated many disease targets and receptor sites that are not yet well understood. Eventually, expansion in the scientific knowledge base should lead to substantial efficiencies in the R&D process for new pharmaceuticals.

The Hatch-Waxman Act: Balancing Innovative and Imitative Competition

The patent system is the public policy instrument designed to balance the trade-offs between property rights protection and imitative competition. Without a well-structured system of global patent protection, neither the research pharmaceutical industry nor the generic industry would be able to grow and prosper, and the rate of new product introductions and patent expirations would decline significantly.

Effective patent life (EPL), defined as patent duration from a product’s market launch date, is an important variable influencing R&D incentives in this industry, because it takes many years to recoup the R&D costs and earn a positive return for a typical new drug introduction. Because firms apply for patents at the beginning of the clinical development process, significant patent protection is lost by the length of FDA approval time. This implies a significant reduction in the effective patent life of drugs relative to the nominal life of 20 years. In light of this, the United States, the European Community and Japan have all enacted patent term restoration laws.

The U.S. law in this regard, the Hatch-Waxman Act, has been in existence since 1984. Hatch-Waxman provides for patent term restoration of time lost during the clinical development and regulatory approval periods, up to a maximum of five years additional patent life. This law also facilitates faster generic product introduction by allowing generic firms to file abbreviated new drug applications, in which generic firms must only demonstrate bioequivalence to the pioneer’s products to obtain FDA approval. Prior to the passage of Hatch-Waxman, generic firms had to submit their own proof of a compound’s safety and efficacy, as well as show bioequivalence.

Under the act, generic firms can also conduct bioequivalence testing.
and FDA submissions in the pre-patent expiration period so that they can enter the market immediately after patent expiration or invalidation. In addition, the Hatch-Waxman Act allows a generic drug manufacturer to file a "Paragraph 4 Certification" challenging the validity of the patent granted to the branded drug, which in turn triggers up to a 30-month stay while the matter is being litigated. If the challenge is upheld, the generic drug gets a 180-day exclusivity period where no other generic drug is allowed to enter.\(^8\)

Grabowski and Vernon (2000) have investigated the effects of Hatch-Waxman on both generic competition and effective patent lifetimes. Figure 2 shows the trends in EPLs by approval year for the new drugs introduced in the first half of the 1990s. This figure indicates that the average EPLs in the 1990s center around an 11- to 12-year range.\(^9\) The mean for all 126 new drug introductions in the 1990-1995 period is 11.7 years with an average Hatch-Waxman extension of 2.33 years. In the last two years of this period, when virtually all of the drugs involve compounds that entered clinical testing after 1984, the average extension is close to three years in length. The mode of the frequency distribution of EPLs for this sample of annual new drug introductions is in the interval of 12 to 14 years.
GENERIC COMPETITION SINCE THE ACT

In contrast with new product introductions, the development costs of generic compounds are relatively modest. In the United States, since the passage of the 1984 Hatch-Waxman Act, generic products need only demonstrate that they are bio-equivalent to the pioneering brand to receive FDA approval. Generic firms can file an Abbreviated New Drug Application (ANDA), a process that takes only a few years and typically costs a few million dollars (CBO 1998 and Reiffen and Ward 2002). Also, the probability of success is very high, as reflected by the fact that many generic firms file to receive FDA approval and enter the market within a short window of opportunity around patent expiration of the pioneer brand.

A distinctive pattern of competitive behavior for generic and brand name firms has emerged in the wake of the 1984 act. First, commercially significant products experienced a large number of generic entrants within a short time after patent expiration, in sharp contrast to what occurred in the pre-1984 period. Also, in the post-1984 period, a strong positive relationship between the size of the market and the number of generic competitors can be noted in accordance with expectations from economic theory.

Second, generic drugs exhibited a high degree of price competition after 1984. The initial generic product entered the market at a significant discount compared to the brand name product, and this discount grew larger as the number of generic competitors for a particular brand name product increased over time. In a study of commercially significant products from 1984 to 1989, Grabowski and Vernon (1992) found that generic prices averaged 61 percent of the brand name product during the first month of generic competition. This declined to 37 percent by two years after entry.

Third, a more rapid rate of sales erosion in brand name products was observed in the case of more recent patent expirations. This is especially so for the top selling drug products which attract the most intensive generic competition. Three recent cases illustrate this phenomenon. Generic enalapril, launched in August 2000 as a substitute for the brand name drug Vasotec®, obtained 66.4 percent of new prescriptions just four weeks after its launch. Generic lisinopril, launched in May 2001 against the brand name drugs Zestril® and Prinivil®, acquired 84 percent of new prescriptions in four weeks. Generic fluoxetine, launched in August 2001 against the brand name drug Prozac®, acquired 74.9 percent of new prescriptions in four weeks.10

The Congressional Budget Office (CBO 1998) has also done an analysis of the economic effects of Hatch-Waxman. As in Grabowski and Vernon's analysis, they found that generic competition has been a powerful force for price competition since 1984. The CBO estimated annual savings of $8 billion to $10 billion to consumers by the mid-1990s. In terms of R&D incentives, however, they found that Hatch-Waxman has had negative effects on the expected returns on R&D. In this regard, they estimated that the act, together with the increased demand side incentives promulgated by managed care organizations in order to utilize generic products in the 1990s, has resulted in steadily accelerating erosion of pioneer-brand’s sales in the period after generic entry.
Overall, price competition and generic utilization have increased dramatically since the Hatch-Waxman Act was passed. In 1984, generic products accounted for approximately 14 percent of all prescriptions. By 2002, the figure was 51 percent. The growth of managed care and other related demand-side changes have been important factors underlying this rapid increase in generic usage. However, the passage of the 1984 act played a critical role by relaxing the regulatory hurdles for generic firms and facilitating higher levels of generic entry.

As discussed earlier, capitalized R&D costs per new drug introductions are influenced by a number of factors. These include out-of-pocket costs at the preclinical and clinical phase, the probability of success for new drug candidates at different stages of the R&D process, and the length of time that it takes to move through all the stages of the R&D process and gain FDA approval. Recent studies of the probability of success and the length of the R&D process for biotech drugs indicate a convergence in these parameters toward the values observed for small molecule pharmaceuticals.

Two initial studies found that success rates for biotech drugs were substantially higher than success rates for new chemical entities (Bienz-Tadmore et al. 1992 and Stuck 1994). In particular, both studies projected success rates for biopharmaceuticals in excess of 50 percent. However, a basic assumption implicit in the methodology of both studies is that success rates for biotech drugs that entered development in the late 1980s and early 1990s are the same as for the biotech drugs that entered development in the early to mid 1980s. This is a very strong, and potentially hazardous, assumption given that 90 percent of the drugs in their samples were still under active testing.

Subsequently, Gosse et al. (1996), analyzed a comprehensive sample of U.S. biopharmaceutical drugs and compared the success rates of older and newer biotech entities. They found dramatic differences in the time pattern of success rates observed for early versus later biotech drug cohorts. In particular, for the investigational new drugs (INDs) filed in the early 1980s,
the success rate for new recombinant entities is 38 percent. For the INDs filed during the late 1980s the success rate was only 10 percent based on approvals to date (i.e., six years after testing). At a comparable point in time, the new recombinant entities of the early 1980s had a success rate of 26 percent. In fact, the success curve of the recent recombinant entities more closely resembles that of new chemical entities rather than that for the early biological entities.

This result is consistent with the history of biotech research in the U.S. The first biological entities introduced into the market were naturally occurring proteins that replaced purified non-recombinant formulations already in general use as established therapies (e.g., insulin and human growth hormone). It is reasonable to expect that recombinant versions of established therapies would have high success rates, once the technology to manufacture these products was proven. Other earlier targets for biotechnology were naturally occurring proteins with well-known and defined physiologic activity (e.g., erythropoietin and filgrastim). As the biotech drugs moved to targets for which limited knowledge existed about clinical and pharmacological profiles, it is reasonable to expect that success rates would fall back toward those of conventional drug entities.

The prospect of a long and uncertain discovery and development period for a new drug is another factor affecting costs and risks in the drug R&D process. The longer the development and approval process, the higher the interest costs, opportunity costs, and the overall capitalized R&D costs of a new drug introduction. Recently, Janice Reichert of the Tufts University Center for the Study of Drug Development has done a historical analysis of clinical development time for successive cohorts of new biopharmaceuticals. She found that recently introduced biopharmaceuticals had much longer clinical development times than earlier introductions. In particular, the cohort of 2000-2001 new biopharmaceutical introductions had a total clinical development time (including FDA approval) of 86 months, versus 53.2 months for 1982-1989 biopharmaceutical introductions.12

Hence, the experience with respect to development times parallels the experience observed with respect to success rates. In particular, there has been a convergence in clinical trial period times observed for new biological and new chemical entities. Of course, the biotech industry is still in the early stages of evolution. It may eventually produce higher success rates and shorter development times as a result of new technologies currently emerging in the discovery period. However, the best evidence at this time shows that biopharmaceuticals, like new chemical entities, are subject to very high rates of attrition and long gestation periods in the clinical development stage.

One aspect in which biopharmaceuticals may differ from small molecule new chemical entities concerns the ease of generic entry when patents expire. To date, there have only been a few patent expirations involving biopharmaceuticals. One case in which there has been entry after patent expiration is that of human growth hormone. However, all entry to
Figure 3:
Present Values by Decile: 1990-1994 NCEs
date has been by other big pharmaceutical firms that have had experience supplying this product in Europe and Japan (Pharmacia, Novo Nordisk and Ares Serono). There are greater hurdles in manufacturing biopharmaceuticals at an efficient scale compared to new chemical entities, and in addition there are greater regulatory requirements for biologicals associated with the manufacturing process (Grabowski and Vernon 1994). These factors may moderate the degree of imitative competition for biopharmaceuticals compared to small molecule chemical entities. Whether or not this is the case will become more apparent when some of the commercially important biopharmaceuticals are subject to patent expiration and potential generic competition in the coming decade.

**Returns on R&D for New Drug Introductions**

Grabowski et al. (2002) have examined the distribution of returns for new drug introductions. This work builds directly on the R&D cost analysis of DiMasi, et al, and considers the sales and net revenues realized over the product life of new drug introductions during the 1970s, 1980s and 1990s. One finding of this work is that the distribution of returns to new drug introductions is highly variable, noting another source of risks for firms developing new drug introductions.

Figure 3 shows the distribution for present value of net revenues (revenues net of production and distribution costs but gross of R&D investments outlays) for new drug introductions between 1990 and 1994. The distribution shows very strong skewness. Roughly one half the overall present value from this sample of 118 compounds is accounted for by the top ranked decile of new drug introductions. The top decile has an estimated after-tax present value that is more than five times the present value of average after-tax R&D costs per approved introduction. Furthermore, only the top three deciles of new drug introductions have present values that exceed average R&D costs.

A major factor underlying the skewed distribution observed in Figure 3 is the level of sales realized by new drug introductions. A few drugs achieve peak sales of several billion dollars and account for a large share of overall revenues. At the other end of the distribution, many compounds achieve peak sales only in the tens of millions of dollars and fail to provide a positive return on investment. Grabowski and Vernon have investigated other periods and time cohorts of new introductions and found that they are characterized by similar patterns (Grabowski et al. 2002).

These returns to R&D analyses confirm that the search for blockbuster drugs is what drives the R&D process in pharmaceuticals. The median new drug introduction does not cover average R&D costs (including allocations for the cost of discovery and the candidates that fall by the wayside). A few top-selling drugs are key in terms of achieving economic success in pharmaceutical R&D over the long run. The large fixed costs of pharmaceutical development and the skewed distribution of outcomes help to explain the clustering of biotech firms at the research stage of the R&D process.
and the large number of alliances between biotech and big pharmaceutical firms at the development and marketing stages.

In Figure 4 (see page 24), the distribution of worldwide sales in 2000 is presented for 30 new biological entities introduced into the U.S. market between 1982 and 1994. All the compounds had been in the market at least seven years, and had progressed beyond the initial rapid growth phase of their life cycle. The sales data presented in Figure 4 indicates that new biopharmaceuticals also exhibit a high degree of skewness, similar to the much larger cohort of new drug introductions.

The high degree of skewness in the outcomes of pharmaceutical R&D projects indicates that there are substantial risks in this endeavor, both for big pharmaceutical firms as well as smaller biotech enterprises. This reflects the dynamic nature of the R&D process, the long time periods from the start of a project to market approval, the unpredictability of clinical trials, as well as regulatory and competitive uncertainties.

Even though many big pharmaceutical firms spend billions of dollars per year on a diversified portfolio of in-house and out-sourced projects, this does not guarantee a stable set of outcomes. If a firm invests in a large diversified portfolio of projects that are more tightly clustered around the mean return (e.g., the so-called "normal" or Gaussian distribution), we expect that returns can be predicted with some confidence. When returns are highly skewed, however, individual companies experience highly volatile outcomes even when they invest in large numbers of independent projects.

To illustrate this point, Grabowski and Vernon examined the new product sales for the U.S. drug companies that spent between $300 and $500 million on their global R&D in the mid-1980s (the top tier group in that period). They found that subsequent new product sales emanating from these R&D efforts varied between $100 million and $3 billion (after seven years of market life) (Grabowski and Vernon 2000).

Finally, it is important to note that the distribution of outcomes from pharmaceutical R&D projects has similar characteristics to many other innovation samples, including venture capital funding of high tech start-ups. In this regard, Scherer, et al, have examined the size distribution of profits from investments in innovation projects using a diverse set of data samples (Scherer et al. 2000). Their analysis included two large samples of high technology venture capital investments, as well as a comprehensive sample of venture backed start-up firms that had their initial public offering in the mid-1980s. A common finding was that the size distribution of profit returns from technological innovation is strongly skewed to the right. As in the case of new drug introductions, the most profitable cases contribute a disproportionate fraction of the total profits from innovation.

Table 1 summarizes the results from four data sets employed in Scherer’s analysis. The first two data sets, assembled by Venture Capital Incorporated and Horsley Keough Associates, involve an analysis of several hundred venture capital firm investments in high tech start-up companies. Scherer’s analysis indicates that roughly 60 percent of the returns, mea-
Table 1: Returns Distribution for Selective Innovation Samples

<table>
<thead>
<tr>
<th>Dataset</th>
<th>Percent of Value From Top Decile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venture Capital (Start-Ups)</td>
<td>62%</td>
</tr>
<tr>
<td>Horsley-Keough (Start-ups)</td>
<td>59%</td>
</tr>
<tr>
<td>1980s IPOs— (1995 Value)</td>
<td>62%</td>
</tr>
<tr>
<td>1990s New Drugs (Grabowski-Vernon)</td>
<td>52%</td>
</tr>
</tbody>
</table>

sured at the time of the final distributions to investors, are realized by the top decile of venture capital projects. At the same time roughly half of the projects in these samples failed to earn positive returns. Similarly, an analysis of the stock market performance of the universe of high tech companies that went public in the mid-1980s found that the top decile of companies realized 62 percent of the sample’s total market value 10 years later. The corresponding value for Grabowski and Vernon’s sample of 1990-1994 new drug introductions is 52 percent. Hence the three samples of risky, high-tech start-up companies exhibit skewed distributions of returns comparable to the pharmaceutical industry.

CONCLUSIONS AND POLICY CONSIDERATIONS

Economic analyses of the R&D process in pharmaceuticals indicate that it is a very costly and risky process, even for large established firms. Most compounds in the R&D pipeline never reach the marketplace. The development process is time consuming and expensive, and the distribution of profits among those products that are marketed is highly skewed. A few blockbuster successes cover the losses on many other R&D investment projects. An important implication for public policy is that reimbursement, regulatory or patent policies that target the returns to the largest selling pharmaceuticals can have significant adverse consequences for R&D incentives in this industry (Grabowski and Vernon 1996).

Many compounds in the top decile of the returns distribution involve the
first mover, or other early entrants, in a new therapeutic class. The family of medicines in a given therapeutic class passes through a well-debated life cycle. There is dynamic competition involving breakthrough, as well as incremental advances, among the branded products within that class. This dynamic competition, in turn, produces substantial consumer surplus and social returns. When the patents for established products expire, consumers also benefit from imitative competition from generic entrants, which provide social benefits in terms of significantly lower prices.

Patents play a critical role for both the level of R&D investment in pharmaceuticals and the timing of generic competition. The Hatch-Waxman Act was designed to balance the trade-offs between these two objectives. In particular, it sought to produce patent lifetimes sufficient to encourage increased levels of R&D investment by innovators while promoting intense price competition by easing entry regulations to generics when patents expire. The degree of generic competition has increased dramatically since the 1984 act was passed, with more than half of all new prescriptions accounted for by generic products in 2002.

The Hatch-Waxman Act has fostered a vigorous generic industry with substantial benefits to consumers from price reductions. However, the CBO’s (1998) analysis of the act found that from the perspective of R&D returns, the much more rapid loss of sales in the period after patent expiration has dominated the patent term restoration aspects of the law. In particular, using Grabowski and Vernon’s analysis of R&D returns as their conceptual frame-

work, they estimated 12 percent lower expected after-tax profits from R&D for the mean new drug compound as a consequence of the 1984 act. While the mean compound is still moderately profitable in their analysis, the increased generic competition since 1984 can have adverse R&D incentives for compounds of above average riskiness or ones with shorter than average effective patent life.

Overall, Hatch-Waxman has provided a relatively balanced approach to the trade-offs between pharmaceutical R&D and generic competition. Improvements on the margin could be considered by policy makers, such as a longer minimum exclusivity period before an ANDA could be filed for new drug introductions (currently five years in the United States but longer in Europe and Japan). Nevertheless, the law has provided a reasonably well-structured system of incentives for both innovative and generic firms. Both R&D investments and generic utilization have increased dramatically in the period since the passage, consistent with the objectives of the act. Some groups have suggested that Congress consider significantly altering or eliminating the patent restoration aspects of the law in order to further increase generic competition in pharmaceuticals. Given the critical role that patents and effective patent life play in terms of R&D incentives for this industry, this would not appear to be a desirable course of action on social welfare grounds.

Notes
1 See, for example, Triplett (2000).
2 In a follow-on study, Silberston categorized three groups of industries for
when patents are essential, very important or less important based on both survey responses and objective analyses (patent and R&D intensity). He concluded that, "The first category consists of one industry only, pharmaceuticals." (Silberston, Z.A. 1987. "The Economic Importance of Patents." The Common Law Institute of Intellectual Property. London.) Edwin Mansfield surveyed the R&D directors of 100 U.S. corporations on what fraction of the inventions they introduced between 1981 and 1983 would not have been developed without patent protection. For pharmaceuticals, the value was 60 percent, while the average across all industries was 14 percent. (Mansfield, E. 1986. "Patents and Innovation: An Empirical Study." Management Science. 32:175.

4 Capitalization takes account of interest payments and foregone earnings from investments of comparable riskiness during the lengthy R&D investment period for a new drug.
5 For data on the trends in effective patent time, see Grabowski and Vernon 2000.
6 Title II of the Waxman-Hatch Act provided for partial restoration of the patent time lost during the clinical testing and regulatory approval periods. A formula for patent term restoration was embedded in the law. In particular, new drugs were eligible for an extension in patent life equal to the sum of the NDA regulatory review time plus one-half of the IND clinical testing time. The law capped extensions at five years and also constrained extensions to a maximum effective patent lifetime of 14 years. Drugs in the pipeline at the time the Act was passed, in September 1984, were limited to a maximum extension of 2 years.
7 For new drug products with little or no effective patent life, generic firms are prohibited from filing an abbreviated new drug application within the first 5 years of the product life. Most European countries prohibit such filing within the first 10 years of market life.
9 This includes any benefits from the international GATT Agreement passed by Congress in 1994 which harmonized U.S. patent laws with foreign countries, including setting the nominal patent life to 20 years from the date of patent application rather than 17 years from the date of patent grant. It does not include any potential benefits of a 6-month extension granted under the FDA Modernization Act in 1997, which can be awarded if the firm does additional testing and gains FDA approval for a pediatric indication.
10 This issue also has been examined using a broad sample of products over


12 These data were obtained in April 2002 from Janice Reichert at the Tufts University Center for Study of Drug Development in Boston, Massachusetts. For further trends and analyses in this regard, see the Tufts Center’s Impact Report, Vol.3, No.6, Nov./Dec 2001.


14 Grabowski and Vernon (2000) found that relatively few new chemical entities are marketed with effective patent lifetimes of less than 10 years.


REFERENCES


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Henry Grabowski has been at Duke since 1972, where he is Professor of Economics and Director of the Program in Pharmaceuticals and Health Economics. He received his undergraduate degree in engineering physics at Lehigh University in 1962 and his doctorate in economics from Princeton University in 1967. He has also served on the faculty of Yale University and held visiting appointments at the Health Care Financing Administration in Washington, DC, and the International Institute of Management in Berlin, Germany. His recent publications have focused on the economics of the research and development process in pharmaceuticals and the costs and returns of new drug introductions.