Name-brand drug competition may have more effect on innovative returns and prices than generics competition.

Between- vs. Within-Patent Competition

BY TOMAS J. PHILIPSON AND CAROLANNE DAI
University of Chicago

ECONOMISTS HAVE LONG APPRECIATED the importance of research and development (R&D) for economic progress. Accordingly, researchers have scrutinized the effects and desirability of stimulating various forms of research and innovative activity through such public interventions as direct R&D tax-incentives, non-profit tax exemptions for research institutions, public financing of R&D activity, and intellectual property regulations (i.e., patent, copyright, and trademark policy).

A substantial body of theoretical work has examined how much innovation intellectual property regulations induce. The analyses have generally assessed the impact of those regulations through their effect on protecting innovative returns from potential imitators who attempt to produce the same product as the innovator.

However, the loss of innovative returns because of "within-patent" competition from imitators through patent expiration is only one way in which innovative returns may be reduced by competition. The other way is through "between-patent" competition from new patents being developed by competitors. A patent only protects an innovator from others producing the same product; it does not provide protection from others producing better products under new patents. For example, in the pharmaceutical industry, within-patent competition after patent expiration stems from so-called generic manufacturers, and between-patent competition through new patents arises from so-called "brand-name" manufacturers engaging in therapeutic competition within disease and drug classes.

Between-patent competition may be as important a limit on innovative returns as within-patent competition, particularly in high-tech fields such as the telecommunications, biotechnology, and pharmaceutical industries. In those industries, which in turn contribute greatly to technological progress and growth, the demand for a given innovation is often destroyed by entry of new, superior products long before the first product's patent expires. In addition, within-patent competition occurs many years in the future and is thus less important for the present value of innovative returns. Therefore, extensive "creative destruction" through between-patent competition leaves less to be subsequently destroyed by "uncreative" within-patent competition.

Public sector stimulation The existence of creative and uncreative competition limits the ability of the public sector to stimulate R&D. Because future innovation limits the rewards to current innovation, intellectual property policies whose purpose is to stimulate R&D may have offsetting effects on innovation. Policies that stimulate R&D not only increase the current incentive to innovate, but also the incentives of producers engaging in between-patent competition. For example, an increase in an R&D tax break would make research cheaper for the innovator, but also imply that the innovator will only be able to enjoy his market advantage for a shorter duration before new patents eliminate it. Existing analyses ignore the effect of between-patent competition and thus give

Tomas Philipson is a professor in the University of Chicago's Harris School of Public Policy Studies. **Carolanne Dai** is a graduate student in the Harris School.
This article summarizes the discussion contained in the paper "The Dual Effects of Intellectual Property Regulations," by Philipson and Frank Lichtenberg, forthcoming in the *Journal of Law and Economics*.

MORGAN BALLARD

misleading implications about the effects and desirability of intellectual property regulations. In fact, because policies that reduce within-patent competition may be offset by between-patent competition, the public sector may not be able to fine-tune R&D.

Given the importance of both within- and between-patent competition, our study attempts to estimate their relative impacts on innovative returns for one of the most R&D intensive industries in the nation — pharmaceuticals. In 1997, R&D intensity (R&D expenditure as a percentage of net sales in R&D performing companies) was three times as high in the "drugs and medicines" industry as it was in the economy as a whole (10.5 percent vs. 3.4 percent). Although the pharmaceutical industry is often mentioned as one in which patents have their standard textbook effects, the relative importance of between-patent or therapeutic competition, rather than within-patent competition from generics, is not well understood in this industry.

Although generic competition may limit innovative returns, we find that less than half of drugs experience generic entry upon patent expiration because between-patent competition accounts for at least as much erosion of innovator returns as within-patent competition caused by patent expiration, and often considerably more. The relative importance of between-patent competition may be even higher in other high-tech industries because the average effective patent length is shorter in pharmaceuticals than it is in other industries.

We use our estimates of the two forms of competition to assess the impact of marginal changes in patent lengths on innovative returns, such as those resulting from the Hatch-Waxman Act for U.S. pharmaceuticals or from the international expansion of patent length from 17 to 20 years. Although the latter represents almost an 18 percent increase in the patent life, it may only increase innovative returns by a couple of percent because of both discounting (the practice of weighting future gains and losses less heavily than those that occur in the present) and between-patent competition. Similarly, the proposed Greater Access to Affordable Pharmaceuticals (GAAP) Act, which attempts to facilitate entry of generic drug companies by accelerating patent expiration, would have little impact on innovative returns and hence little or no effect on the incentives for brand-name drug manufacturers to engage in R&D.

WITHIN- VS. BETWEEN-PATENT COMPETITION

Consider the innovative returns of a patent with a certain patent length. It faces between-patent competition from a number of competing patents during the patent period, and within-patent competition from a number of imitating competitors after the patent has expired. We assume profits in each period to be a function of market structure and hence proportionate to the number of both types of entrants given the entry rates of between- and within-patent competition and discount rates before and after the patent expires.

The value of the innovation can then be seen as a function of the extent of within- and between-patent competitions. Both within- and between-patent competition lower the innovative return. A common argument about the value of patents is that imitation reduces the value of creativity – indeed, that is the most frequent rationale offered for tolerating the distortions

imposed by patent protection in the first place.

However, the opposite is also true. Imitation (within-patent competition) is reduced by creativity (between-patent competition) for two related reasons. First, between-patent competition reduces the profits to be sought after by within-patent competition. Second, between-patent competitors compete with within-patent competitors after expiration. Therefore, within-patent competition has a smaller effect on innovative returns as between-patent competition grows larger.

This interaction implies that changes in patent length may not affect R&D incentives in quantitatively important ways because of the existence of substantial between-patent competition. For example, consider a situation where there is a five percent discount rate per year and a 15 percent profit depreciation per year because of between-patent competition. The depreciation of patented profits would then occur at a rate of 19 percent per year. In that case, even when there are no profits to be had once the patent has expired, the value of the innovative return of a 17-year patent is close to 97 percent of the value of a patent with infinite length. Our research suggests that recent international agreements to extend patent lives from 17 to 20 years – close to an 18 percent increase in the patent life – have only increased innovative returns by a couple of percent.

Public sector effects Consider such public policy R&D stimuli as a tax break that lowers the marginal cost of R&D or government funding of National Institutes of Health research that complements private R&D. In a world in which only within-patent competition existed, such policies would unambiguously stimulate R&D.

But in a world with between-patent competition, the net effect of a policy that appears to encourage R&D is less certain because of the indirect or unplanned effects of between-patent competition. The indirect effect may be offsetting or reinforcing, depending upon how between-patent competition affects profits. The offsetting case is likely to occur when between-patent competition occurs through R&D on substitute products, e.g., different cholesterol-lowering drugs. The reinforcing case is likely to occur when between-patent competition occurs through R&D on complementary products, e.g., acne drugs – topical creams and antibiotics. The complementary case may not only operate through the demand side (e.g., demand for antibiotics will most likely induce demand for topical creams), but may be present through producer activities such as spillovers in advertising (e.g., direct-to-consumer advertising for antibiotics will also benefit producers of topical acne creams because it generates foot traffic into physicians' offices and expands the market for all acne drugs).

In those cases in which the indirect effect of between-patent competition offsets the direct effect of within-patent competition, the net effect of a patent-length extension is only a marginal increase in innovative returns. The offsetting or neutralizing effects of between-patent competition may imply that it is very difficult for governments to "fine-tune" or manipulate R&D efforts and economic growth.

TABLE 1

A Matter of Time

Extent of within- and between-patent competition, by age of the drug, 1982-2001.

Drug age	Average number of producers of a drug	Average number of drugs within a drug's class
0	1.02	24.9
5	1.17	27.9
10	1.91	31.5
14	2.78	33.9

The particular case of pharmaceutical innovation may illustrate those offsetting effects. The Food and Drug Administration regulates testing and marketing of drugs and devices, and thus lowers the probability of success by rejecting some innovation and increases the cost of R&D beyond the level that would occur in an unregulated world through distortions imposed on the cost of clinical trials. Conventional analyses that consider only within-patent competition have concluded that FDA regulation discourages innovation. But such a conclusion ignores the negative effect of FDA regulation on between-patent competition. By reducing between-patent competition, FDA regulation serves as an improved patent by keeping out low-quality innovators that could have competed with high-quality innovators.

EMPIRICAL ANALYSIS

In this section, we attempt to evaluate the empirical importance of the two sources of competition for the U.S. pharmaceutical industry where within-patent competition after patent expiration is from generic manufacturers and between-patent competition is from brand-name manufacturers engaging in therapeutic competition within a given disease class. We document the entry of both forms of competition as a function of the age of the patent, note the effects such entry has on innovative returns, and decompose the share of the present value of an innovation lost to the two forms of competition. Our analysis refers to competition between patents as competition between drugs in the same class (e.g., competition between Lipitor, Zocor, and other cholesterol-lowering drugs). We refer to competition within patents as competition between producers of the same drug (e.g., competition between Andrx, Aventis, Biovail, and other producers of the drug diltiazem).

TABLE 2

Generic Entry

Market entry for drugs containing amiodarone hydrochloride.

Year Approved	Applicant
1985	Wyeth Ayerst
1998	Copley Pharm
1998	Eon
1998	Upsher Smith
1999	Alphapharm
1999	Novopharm

Average rates of entry Table 1 presents data on the typical extent of within-patent competition (the average number of producers of a drug) and between-patent competition (the average number

of drugs within a class) by age of the drug (number of years since FDA approval) during the period 1982-2001. Table 1 reveals that there is a substantial amount of between-patent competition for a drug even upon entry; approximately 25 drugs already exist in the class, as well as through additional entry while on patent. In contrast, within-patent competition increases only by less than a single drug during the first 10 years.

Within-patent entry Our first source of data on the general pattern of within-patent entry in the pharmaceutical industry is the FDA's *Orange Book*. It lists all approved prescription drugs, including brand-name drugs that represent between-patent competition and generic drugs that represent within-patent competition. For each of the 1,520 ingredients identified in the Approved Drug Products file of *The Orange Book*, we determined the first date at which a product containing that ingredient was approved for marketing. As an example, consider the data in Table 2 for the antiarrhythmic drug amiodarone hydrochloride.

For each drug first approved in 1982 or later, we computed the number of producers representing the within-patent entrants that were approved to market a drug. Regression analysis was performed to determine the typical rates of increase in the number of entrants over the life cycle of a drug. The length of a pharmaceutical patent has historically been 17 years, but it was recently extended to 20 years. The data suggest that a drug is fairly well protected from early entry, after which the probability of entry rises exponentially as the drug's age approaches the statutory patent length. However, at the time of patent expiration, the average probability of within-patent competition is less than 50 percent.

Between-patent entry To assess between-patent competition, it is important to define the relevant markets in which patents compete. Drugs are a very useful product market to study in this respect because the disease categories into which therapeutic competition occurs are relatively well defined compared to other markets. *The National Drug Code Directory* was used to define therapeutic classes in which patents compete. It serves as a universal product identifier for human drugs, and uses a general therapeutic classification scheme for the drug products reported to the FDA under the provisions of the Drug Listing Act. We first linked two *National Drug Code* files to obtain a mapping from drugs (ingredients) to drug classes, and then linked the list of drug classes to the list of drugs obtained from *The Orange Book*, which included the FDA approval date of the drug. The resulting list was subsequently sorted by drug class and approval date. The final list shows the history of new drug approvals by class.

Using that information, we computed the number of drugs in a given class, representing the between-patent competition, by age of the drug. We used regression analysis to estimate the average number of drugs approved in a class (between-patent entrants) and applicants approved to market a drug (within-patent entrants), given the age of a drug. The results are reported in Table 3 and

TABLE 3

Coming of Competition

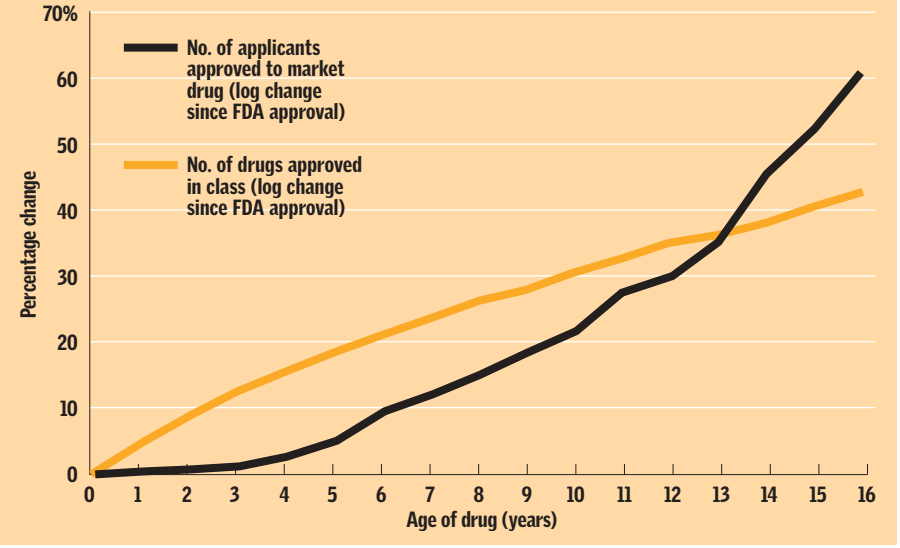
Number of drugs approved in class, and number of applicants approved to market a drug, by drug age, 1982-2001.

Age of drug (years)	No. of applicants approved to market (log change since FDA approval of drug)	No. of drugs approved in class (log change since FDA approval of drug)
0	0.0%	0.0%
1	0.4%	4.9%
2	0.7%	9.0%
3	1.2%	12.6%
4	2.7%	15.7%
5	5.3%	18.7%
6	9.5%	20.9%
7	11.9%	23.7%
8	15.0%	26.2%
9	18.5%	28.0%
10	21.4%	30.4%
11	27.4%	32.5%
12	30.1%	34.6%
13	35.1%	36.2%
14	45.4%	37.9%
15	52.3%	40.4%
16	60.6%	42.5%

FIGURE 1

Enter the Competition

Number of drugs approved in class (between-patent competitors), and number of applicants approved to market drug (within-patent competitors), by drug age, 1982-2001.



plotted in Figure 1.

In the first three years, the average number of applicants increases by just 1.2 percent, while the average number of drugs in the class increases by 12.6 percent. However, in the next three years, there is a significant acceleration in the average number of applicants and slight deceleration in the average number of drugs in the class. By year six, the average number of applicants is 9.5 percent larger than it was initially, and the average number of drugs in the class has increased by 20.9 percent. The increase in the number of drugs in the class remains higher than the increase in the number of applicants until year 14.

TABLE 4

Effects of Competition

Estimates of the effects of between- and within-patent competition by product type (t-statistics in parentheses).

	Innovator drugs			Non-innovator drugs		
Dependent variable	**No. of units**	**No. of prescriptions**	**Dollar value**	**No. of units**	**No. of prescriptions**	**Dollar value**
Regressor:						
Ln N (between-patent competitors)	-0.194 (6.31)	-0.190 (7.80)	-0.175 (6.25)	-0.104 (5.44)	-0.080 (4.59)	-0.077 (5.10)
Ln N (within-patent competitors)	-0.068 (3.98)	-0.077 (5.71)	-0.081 (5.25)	-0.240 (13.46)	-0.256 (15.79)	-0.248 (17.59)

In the first 13 years of a drug's life, and especially in the earlier years, the number of between-patent competitors in the drug's class typically increases more, in percentage terms, than the number of within-patent competitors approved to market the same drug. The fact that the rate of between-patent entry is higher does not necessarily mean that it has a larger impact on innovator sales than within-patent entry. In the next subsection, we will estimate the effects of both forms of patent competition on the sales of a new drug.

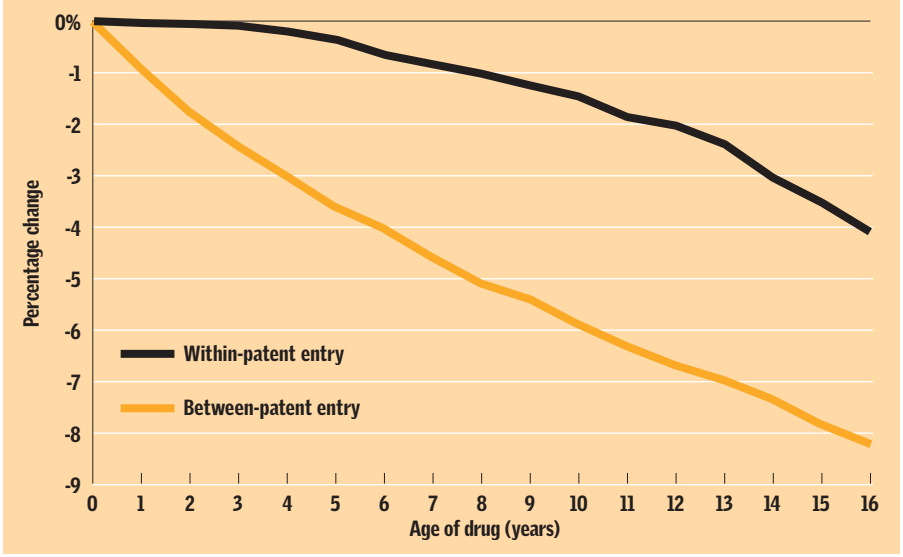
Effects of entry Ideally, to estimate the effects of between- and within-patent competition, one would like to have a complete set of longitudinal data on innovators' sales, by product. Unfortunately, we were unable to obtain data on sales to all customers. However, comprehensive data on Medicaid sales during 1996-1999 are available from Medicaid State Drug Utilization files published by the Centers for Medicare and Medicaid Services (formerly the Health Care Financing Administration). Evidence suggests that the Medicaid program accounts for a significant share of total U.S. pharmaceutical sales, and that drugs purchased under Medicaid are fairly representative of all U.S. drug transactions, at least in terms of price. Therefore, estimates of the impact of between- and within-patent competition on Medicaid sales are likely to be informative about their effects on pharmaceutical sales in general.

Table 4 presents the estimates of the effects of between- and within-patent competition by product type (innovator vs. non-innovator) from our regression analysis, which assumed that there are diminishing marginal effects of entry on incumbent sales, e.g., the first entrant's sales are reduced more by entry of a second firm than they are by entry of a third firm. The first column indicates that both kinds of entry reduce the growth of innovator sales, but the effect of between-patent entry is 2.5 times as large as the within-patent entry effect. The second and third columns reveal the similar effect of both types of entry on the number of prescription and growth in total dollar amount reimbursed.

FIGURE 2

Weakening Sales Growth

Estimated reduction in innovator sales growth from within- and between-patent entry.

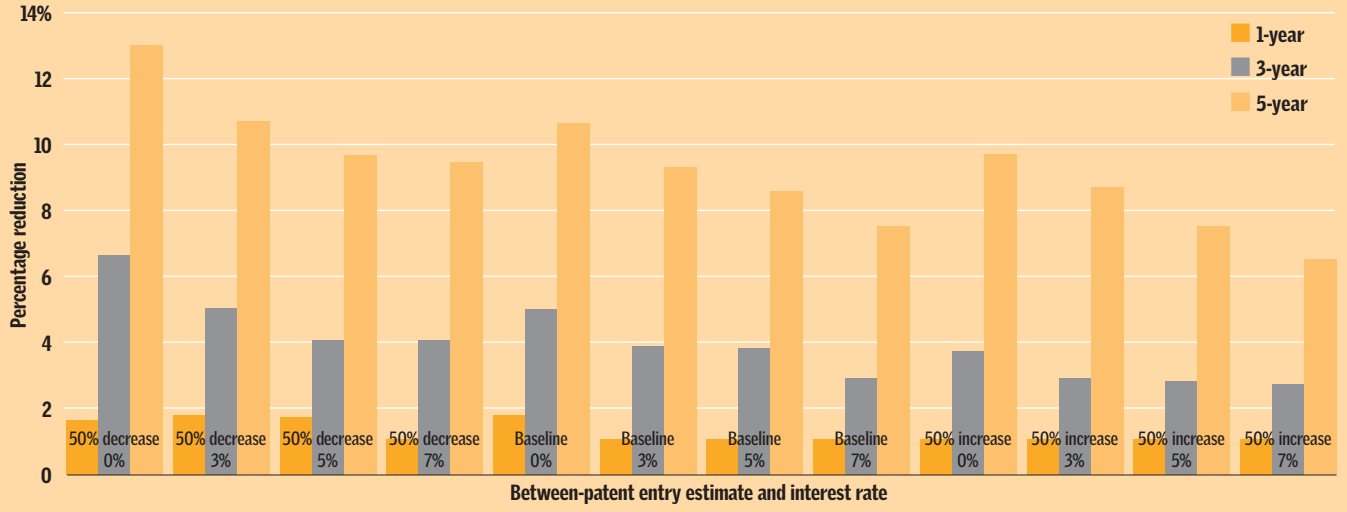


We can estimate the year-by-year reductions in innovator sales growth from between- and within-patent entry by combining the estimates from Table 3 and the first column of Table 4. The estimated reductions in innovator sales growth are plotted in Figure 2. The estimates imply that throughout the first 16 years, and especially in the early years, between-patent entry reduces innovator sales growth much more than within-patent entry. After five years, between-patent

FIGURE 3

Cut in the Profits

Estimated percentage reductions in present discounted value of innovator sales resulting from one-year, three-year, and five-year acceleration of patent expiration.



entry has reduced innovator sales growth by 3.6 percent, while within-patent entry has only reduced sales growth by 0.4 percent. At 10 years, the estimated reductions are 5.9 percent and 1.4 percent, respectively. That gap begins to narrow after 13 years, but in year 16, within-patent entry has still reduced sales growth less than between-patent entry: 4.1 percent vs. 8.2 percent.

Decomposing loss The estimates plotted in Figure 2 can be used to calculate the effects of between- and within-patent entry on the present discounted value of sales during those years, evaluated at age zero, i.e., the date of FDA approval. Consider the counterfactual sales in the absence of any entry (between- and within-patent entry at all ages was set to zero). Now, assume that annual sales were $1,000 for all ages until expiration at year 16. Use the estimated entry rates (from Table 3) multiplied by their estimated effects on sales (from the first column of Table 4) to calculate two new sales profiles by age – one when there is only within-patent competition and another when there is only between-patent competition. Our estimates imply that within-patent entry alone reduces sales in years five, 10, and 15 to $993, $943, and $828, respectively. In comparison, between-patent entry alone reduces sales in those same years by a corresponding $887, $686, and $476. In other words, between-patent entry reduces sales in year 15 by more than twice as much as within-patent entry.

Using a five percent interest rate, we estimate that within-patent entry alone reduces the present discounted value of years 0-16 sales by four percent ($11,313 vs. $11,838), and that between-patent entry alone reduces the present discounted value of years 0-16 sales by 17 percent ($9,420 vs. $11,838). Between-patent entry has about four times as large an effect on the present discounted value of years 0-16 sales as within-patent entry. This finding is not very sensitive to the choice of interest rate. Thus, our estimates suggest that between-patent competition is more important in affecting this measure of an innovative return than is within-patent competition.

Implied effects We use our estimates of the impact on innovative returns for the two forms of competition to assess the effect of marginal changes in patent lengths on innovative returns, such as those resulting from the Hatch-Waxman Act for U.S. pharmaceuticals or from the international expansion of patent lives from 17 to 20 years. More precisely, suppose that the within-patent entry profile in Figure 2 was shifted to the left by one year, three years, or five years. We assume that after 16 years, the within-in patent entry continues to decline by -0.8 percent per year. The effect of that shift on the present discounted value of innovator sales depends on the joint discounting induced by the rate of between-patent entry and the rate of interest.

Now, consider three different sets of values of between-patent entry: baseline as estimated in Figure 2, 50 percent decrease from baseline, and 50 percent increase from baseline. Also, consider four different interest rates: zero, three, five, and seven percent. Figure 3 depicts the estimated percentage reductions in present discounted value of innovator sales resulting from the one-year, three-year, and five-year acceleration of patent expiration under the different scenarios. A useful upper bound on the loss (the percentage reduction in the present discounted value of innovator sales) is the corresponding percentage reduction in the patent life itself. However, as seen from Figure 3, often the actual loss is far below that upper bound.

Those results also may demonstrate the potential consequences of the GAAP Act, passed by the Senate in July 2002, which would facilitate generic entry by limiting the availability of 30-month stays to one per drug per generic application. Under the Hatch-Waxman Act, a generic drug company may file for a Paragraph IV certification in order to market its generic drug under circumstances when patent protection has not expired but the generic company claims that the patent is invalid or that its product does not infringe the patent. Generic drug

companies attempt to be the first to file Abbreviated New Drug Applications (ANDAs) with Paragraph IV certification because the rules make them eligible for a 180-day period of market exclusivity. During that period, the FDA may not approve other ANDAs for the same drug. The exclusivity period motivates generic drug companies to innovate around patents for brand-name drug products listed in *The Orange Book*. During that time, a generic drug can be sold at a price only slightly lower than that of the brand-name product, generating large profits.

When a Paragraph IV ANDA is filed, the brand-name drug company almost always sues the generic company for patent infringement. That action automatically triggers a 30-month stay, during which the FDA may not act on the application. Through strategic timing of *Orange Book* listing of later-issued patents on the drug under dispute, brand-name drug companies can obtain multiple 30-month stays, thereby delaying generic entry prior to patent expiration. (See "Closing the FDA's Orange Book," Winter 2001.)

The GAAP Act would effectively accelerate patent expiration and increase within-patent competition. As shown by Figure 3, a three-year reduction in patent length with baseline between-patent entry rates and a five percent interest rate would decrease the present discounted value of innovator sales by only four percent. That reinforces our previous result, suggesting that between-patent competition is much more important in affecting innovative return and acts to moderate the effect of within-patent competition. Decreasing the baseline between-patent entry rates by 50 percent will magnify the effect of within-patent competition on the present discounted value of innovator sales, whereas the effect is dampened with a 50 percent decrease. Within-patent competition has a smaller effect on innovative returns as the extent of between-patent competition grows larger.

CONCLUSION

A patent protects an innovator from others producing the same product, but it does not protect the innovator from others producing new products under new patents. Thus, the innovator faces two sources of potential competition: within-patent competition that results from production of the same product, and between-patent competition that results from production of other patented products. Previous analyses have focused on the effects of intellectual property regulations on within-patent competition. We compared the relative magnitudes of the two sources of competition in limiting innovative returns in the U.S. pharmaceuticals market.

Our results suggest that between-patent competition, most of which occurs while a drug is under patent, affects the returns to innovators at least as much as within-patent competition, which cannot occur until a drug is off patent. The reduction in the present discounted value of the innovator's sales from between-patent competition appears to be at least as large as the reduction from competition within patents, and maybe much larger. This implies that the statutory monopoly awarded through a patent does not always confer great monopoly power in the usual sense of being able to increase price without substantial substitution.

Although the effects of limiting within-patent competition may be small, restrictions on between-patent competition may have large effects. For example, the U.S. Orphan Drug Act of 1983 added a seven-year exclusivity right to a class of drugs for rare diseases, in addition to further tax breaks for R&D expenditure. (See "The Blessed Monopolies," Winter 2001.) The policy uniquely reduced between-patent competition without the offsetting effects found with other types of R&D stimuli. The Orphan Drug Act dramatically increased both R&D spending and entry of orphan drugs – facts that may be a testament to the relative importance of between-patent competition in eliminating innovative returns. R

READINGS

- "The Economics of Invention Incentives: Patents, Prizes, and Research Contracts," by Brian Wright. *American Economic Review*, Vol. 73 (1983).
- "How Broad Should the Scope of Patent Protection Be?" by Paul Klemperer, *RAND Journal of Economics*, Vol. 21 (1990).
- "How Effective Are Fiscal Incentives for R&D? A Review of the Evidence," NBER Working Paper No 7098, by B. Hall and J. Van Reenen. Cambridge, Mass., 1999.
- "Information, Marketing, and Pricing in the U.S. Antiulcer Drug Market," by Ernst R. Berndt, Linda Bui, David R. Reiley, and Glen L. Urban. *The American Economic Review*, Vol. 85, No. 2 (1995).
- "Longer Patents for Increased Generic Competition in the U.S.: The Waxman-Hatch Act after One Decade," by Henry Grabowski and John Vernon. *PharmacoEconomics*, Vol. 10 (1996).
- "A Model of Growth through Creative Destruction," by P. Aghion and Peter Howitt. *Econometrica*, Vol. 60, No. 2, (1992).
- "On The Division of Profits in Sequential Innovation," by Jerry Green and Suzanne Scotchmer. *RAND Journal of Economics*, Vol. 26 (1995).
- "On the Performance of Patents," by Kenneth Judd. *Econometrica*, Vol. 53 (1985).
- "Optimal Patent Length and Breadth," by Richard Gilbert and Carl Shapiro. *RAND Journal of Economics*, Vol. 21 (1990).
- "Patents as Information Transfer Mechanisms: To Patent or (Maybe) Not to Patent," by Ignatius Horstmann, Glenn MacDonald, and Alan Slivinski. *Journal of Political Economy*, 1993.
- "Patents as Options: Some Estimates of the Value of Holding European Patent Stocks," by Ariel Pakes. *Econometrica*, Vol. 54 (1985).
- "Patent Policy and Costly Imitation," by Nancy Gallini. *RAND Journal of Economics*, Vol. 23 (1992).
- "Pharmaceutical Innovations and Market Dynamics: Tracking Effects on Price Indexes for Antidepressant Drugs," by Ernst R. Berndt, Iain M. Cockburn, and Zvi Griliches. *Microeconomics*, 1996.
- "Protection Early Innovators: Should Second-Generation Products be Patentable?" by Suzanne Scotchmer. *RAND Journal of Economics*, Vol. 27 (1996).
- "Strategic Pricing of New Pharmaceuticals," by J.Z. Lu and W.S. Comanor. *Review of Economics and Statistics*, Vol. 80, No. 1 (1998).