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EUROPEAN PHARMACEUTICAL PRICE REGULATION, FIRM PROFITABILITY,
AND R&D SPENDING

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ABSTRACT

EU countries closely regulate pharmaceutical prices whereas the U.S. does not. This paper shows how price constraints affect the profitability, stock returns, and R&D spending of EU and U.S. firms. Compared to EU firms, U.S. firms are more profitable, earn higher stock returns, and spend more on research and development (R&D). Some differences have increased over time. In 1986, EU pharmaceutical R&D exceeded U.S. R&D by about 24 percent, but by 2004, EU R&D trailed U.S. R&D by about 15 percent. During these 19 years, U.S. R&D spending grew at a real annual compound rate of 8.8 percent, while EU R&D spending grew at a real 5.4 percent rate. Results show that EU consumers enjoyed much lower pharmaceutical price inflation, however, at a cost of 46 fewer new medicines introduced by EU firms and 1680 fewer EU research jobs.

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1. Introduction

European Union (EU) countries closely regulate pharmaceutical prices in various ways, while the United States (U.S.) does not. EU consumers clearly benefit because they often pay lower prices than U.S. consumers for the same medicines. But few government agencies or academic studies examine the less apparent costs of price regulation. One exception is Campa and Hernando (2004), who show that EU mergers of regulated firms produce significantly less value than mergers of unregulated firms. The EU also regulates the conditions for acceptable mergers and acquisitions. Aktas, de Bondt, Levasseur, and Schmitt (2001) and Aktas, de Bondt, and Roll (2004) show that these conditions negatively affect the firms involved.

Our paper studies how EU pharmaceutical price regulation affects EU firms compared to U.S. firms, and the indirect costs to the EU. Although many pharmaceuticals are sold worldwide, EU (U.S.) firms typically sell proportionately more in the EU (U.S.) (see Vernon, 2005). The direct consequence of EU price regulation is that firms selling more in the EU could be less profitable. An indirect consequence could be reduced research and development (R&D) spending, fewer research jobs, and fewer new medicines introduced by EU firms.

The first part of this paper illustrates the average effects of EU price regulation on EU firms compared to U.S. firms. We show that EU pharmaceutical firms are less profitable, spend less on R&D, and earn smaller stock returns than U.S. firms. The EU firms' relatively poor profitability and stock returns are consistent with Doukas and Switzer (1992), who show that profitability and stock prices are positively associated with R&D spending. Reduced EU R&D spending and lower stock returns are costs borne

by EU citizens because they imply fewer well-paid research jobs and lower wealth for EU stockholders.

The strength of this analysis is that it illustrates the costs and potential policy implications of EU price regulation. Although policymakers may care little about pharmaceutical stockholders' low returns, they may be interested in the negative effects that lower EU R&D spending has on high-tech employment and innovation. One weakness of this analysis is that it compares average or aggregate figures for EU and U.S. firms. This obscures some of the effects of EU price regulations. For example, some U.S. (EU) firms could actually be more (less) affected by EU price regulations because they happen to sell more (less) in the EU than in the U.S. Indeed, all firms selling pharmaceuticals in the EU are somewhat affected by EU price regulation.

The second part of the paper examines the general effects that EU regulation has on pharmaceutical R&D spending by U.S. or EU firms. This issue could be studied easily if most firms reported sales and R&D spending by geographic area. Unfortunately, relatively few firms publicly report sales by geographic area, and almost none report R&D expenses by geographic area. Our alternative approach relates each firm's standardized sales to pharmaceutical price indexes. These indexes capture the level of price regulation in each geographic area over time. The relations between a firm's sales and these indexes capture the relative sensitivity of its sales to changes in the indexes. Firm sensitivities are then cross-sectionally related to their average R&D spending. Firms with greater sales sensitivity to the EU (U.S.) price index are expected to spend less (more) on R&D.

The notion that firms subject to greater price controls would spend less on R&D seems straightforward; however, few have studied this relation. One recent study by Giaccotto, Santere, and Vernon (2005) shows that real U.S. pharmaceutical prices and industry-level U.S. pharmaceutical R&D growth are positively related. Our results support theirs using firm-level data from both U.S. and EU firms.

The last part of the paper estimates the costs to the EU of price controls over the last 19 years. We also project potential future costs for the EU, assuming that it retains its current regulatory environment, and for the U.S., assuming that it adopts EU-type regulation over time. Costs are estimated in terms of slower growth in R&D spending, fewer research jobs, and fewer new medicines. We estimate these costs with a variety of growth models. We acknowledge that price controls provide benefits to current consumers, but focus on costs because they have received less attention from researchers and policymakers.

We project costs for the U.S. because EU-type price regulations are gaining popular support. For example, many in the U.S. have called for large-scale reimportation of pharmaceuticals from price-regulated countries like Canada (e.g., Dorgan-Snow U.S. Senate Bill, S.334). Reimportation is an indirect method of price control which is similar to European parallel trade.¹ Other more direct forms of EU-type price regulation have been proposed in the U.S., including several provisions in President Clinton's Health Security Act. In August 2006, California legislators passed the Prescription Drug

¹ Parallel trade is a more general term than reimportation because it refers to any product trade that occurs after the original manufacturer sells the product. For example, product manufactured in Germany, sold to an agent in Spain, and then resold by the agent in Spain to an agent in England is parallel trade. Reimportation fits the more common situation in the U.S. where a U.S. manufacturer sells to a Canadian agent, who then resells to another agent in the U.S.

Initiative, requiring manufacturers to discount pharmaceuticals by between 40 and 60 percent for low-income state residents.

Our results show that EU policy has kept pharmaceutical price inflation equal to average consumer price inflation over the last 19 years, with real costs of about \$5 billion in foregone R&D spending, 1680 fewer research jobs and 46 foregone new medicines. Prospective long-horizon costs for the EU are estimated at between ten and 20 times these costs, with potential U.S. costs about twice the EU's long-horizon costs.

This paper is organized as follows. Section 2 illustrates the difference between U.S. and EU pharmaceutical price inflation. Section 3 compares U.S. and EU firms' profitability, stock return performance, and R&D spending. Section 4 illustrates the differences in U.S. and EU R&D spending growth over the 1986-2004 period using data on U.S.-only and EU-only R&D spending. Section 5 tests the relation between pharmaceutical pricing in the EU and U.S. and R&D spending. Section 6 translates the observed slower growth of R&D spending into foregone R&D spending, fewer research jobs, and fewer new medicines. Section 7 concludes the paper.

2. European and U.S. Pharmaceutical Prices

EU pharmaceutical price regulations take various forms, and many countries use more than one. Vernon (2003) describes the different forms adopted by each EU-member. Most European countries have stated that their pharmaceutical policy goal is to keep pharmaceutical price increases at or below the general rate of consumer price inflation. Although this goal is politically attractive, economic efficiency could easily

justify real pharmaceutical price increases because pharmaceutical demand rises more than proportionately with income.

U.S. pharmaceutical prices are relatively unregulated, but have not been immune to political pressures. In 1993, the Clinton Administration proposed a Health Security Act that included regulations with the stated purpose of keeping pharmaceutical price increases at or below average consumer price inflation. In response, 21 large pharmaceutical firms pledged to keep price increases below average consumer price inflation, perhaps as a way to preempt direct regulation.²

One way to assess the degree to which European regulation or U.S. political pressure have affected pharmaceutical prices is to compare real pharmaceutical price indexes for the EU and U.S. Figure 1 illustrates real growth of pharmaceutical prices for the U.S. and Europe from 1986 to 2004. For each year, the pharmaceutical price index is divided by the consumer price index for all items, and these real index numbers are compounded year to year, with 1986 as the base year.³

Clearly, European regulations have effectively kept pharmaceutical prices from rising faster than general consumer prices. Over the 19 year period, they never rose more than a few percentage points faster than general consumer prices. In contrast, U.S. real pharmaceutical prices increased in almost every year. Real price increases moderated starting in 1993, around Clinton's proposed price regulations (see Ellison and Mullin, 2001). Prices also moderated in 2000 and 2004, just before the presidential elections.

² The firms are Abbott Labs, Bristol-Meyers Squibb, Eli Lilly, Glaxo, Johnson & Johnson, Merck, Pfizer, SmithKline Beecham, Warner-Lamber Wyeth-Ayerst (American Home Products) Ciba-Geigy, Dupont-Merck, G.D. Searle, Genentech, Hoechst-Roussel, Hoffmann-La Roche, Knoll, Marion Merrell Dow, Syntex, Upjon, and Zeneca.

³ U.S. pharmaceutical and CPI (all items price 1982-84 =100) indexes are from the Bureau of Labor Statistics. EU CPI is from Eurostat Harmonized Indexes of Consumer Prices (all items). The EU pharmaceutical price index is from Eurostat starting in 2001 and compiled from OECD Health Data 2003 for the years before 2001.

Tessoriero (2004) suggests that these price moderations reflect firms' efforts to limit political support for campaign platforms that include pharmaceutical price regulations. The relative growth of U.S. pharmaceutical prices continues to be a political flashpoint, however, much like high oil or utility prices.⁴

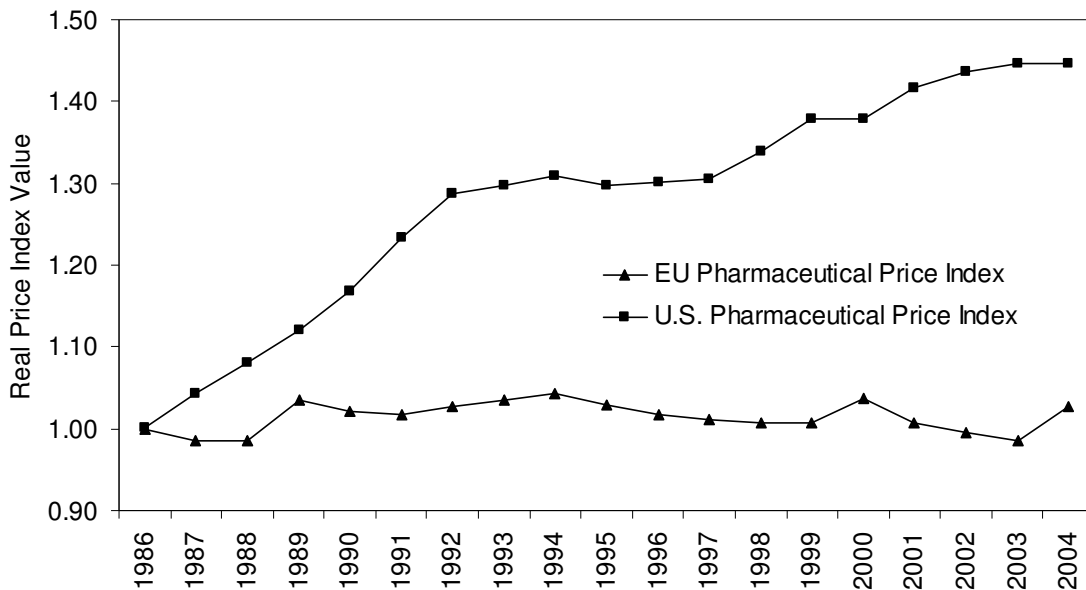


Fig. 1. Cumulative real pharmaceutical price inflation for the EU and U.S., with base year of 1986 = 1, computed by dividing the pharmaceutical price index by the consumer price index (all items).

⁴ A search of the Wall Street Journal for articles that discussed average pharmaceutical price inflation compared to consumer price inflation produces only three articles from 1984 until 1992. Between 1992 and 1993, 12 such articles appeared, and from 1994 through 2005, 42 articles appeared.

3. EU versus U.S. Pharmaceutical Firms' Profitability, Stock Returns, and R&D

Given the EU's restrictive price regulations, one would expect EU firms to be more negatively affected than U.S. firms because proportionately more of their revenue is likely to come from the EU. Unfortunately, few firms report comprehensive data on the geographic distribution of firm sales. Compustat Segments database includes sales by geographic area for firms that report it in their financial statements after 1997. Between 1998 and 2004, 43 (13) U.S. (EU) firms report separate U.S. and EU sales. These data cover only about 40 percent of the firms in our sample. Nevertheless, they show that on average U.S. (EU) firms generated 76 (53) percent of combined U.S. plus EU sales from the U.S. This proportion is stable across years for the U.S. firms, with 76 percent in both 1998 and 2004, and only slight variations in other years. But the proportion for EU firms increases consistently from 43 percent in 1998, to 57 percent in 2004. This illustrates how EU firms' sales have recently shifted toward the U.S., perhaps because the U.S. offered better pricing than the EU during the period.

Table 1 shows how EU firms' profitability and R&D spending compares with that of U.S. firms. To be included in this analysis, a firm had to have at least five years of data in the Compustat Global Industrial/Commercial database between 1993 and 2004 (1993 is the first year available on the database). In addition, the firm must have sales equal to at least ten percent of its assets. Because this study focuses on the effects of price regulation on firm sales and R&D spending, we require that a firm has a minimal amount of product sales.⁵ This condition is also important because each firm's sales sensitivity to

⁵ These filters tend to eliminate small and young firms with few sales. Because the following results are size-weighted, including these firms has little effect on the results.

EU and U.S. price indexes must be estimated. All figures are translated into dollar amounts using Compustat's Currency database.

Profitability is measured by operating income standardized by total firm assets and the intensity of firm R&D is measured by R&D spending divided by total firm assets.⁶ For each year, each firm's profitability and R&D intensity is computed, and a weighted average is calculated for U.S. and EU firms, respectively. The weight placed on each U.S. (EU) firm's profitability or R&D intensity equals the ratio of its total assets to the total assets of all U.S. (EU) firms with data in the particular year.

Table 1

Comparison of EU and U.S. Firms' Profitability and R&D Spending from 1993 to 2004

Year	Number of Firms		Oper. Inc./ Total Assets		R&D / Total Assets	
	U.S.	EU	U.S.	EU	U.S.	EU
1993	77	15	0.193	0.113	0.100	0.084
1994	93	19	0.165	0.108	0.083	0.080
1995	110	20	0.167	0.122	0.090	0.090
1996	120	24	0.173	0.130	0.093	0.083
1997	133	28	0.179	0.120	0.100	0.076
1998	143	30	0.179	0.136	0.104	0.089
1999	132	35	0.190	0.100	0.099	0.079
2000	112	38	0.193	0.107	0.098	0.091
2001	113	38	0.175	0.112	0.107	0.086
2002	112	37	0.166	0.122	0.100	0.099
2003	104	32	0.134	0.148	0.095	0.103
2004	96	30	0.135	0.144	0.085	0.107

Table 1 shows that U.S. firms are more profitable than EU firms in each year except 2003 and 2004. For the 1993-2004 period, U.S. firms averaged 17.1 percent

⁶ We follow Eberhart, Maxwell, and Siddique (2004) who use assets to standardize R&D. Using sales to standardize does not materially change the results.

profitability compared to 12.2 percent for EU firms. The 4.9 percentage point difference is highly significant using a two-tailed t-test (t-stat = 6.85). U.S. firms have greater R&D intensity in all years except 1995, 2003 and 2004. For the 1993-2004 period, U.S. firms averaged 9.6 percent R&D intensity compared to 8.9 percent for EU firms. The 0.7 percent difference is significantly different from zero using a two-tailed t-test (t-stat = 2.07).

These results show that U.S. firms surpass EU firms in average profitability and R&D intensity, although this changed in 2003-2004. U.S. firms' profitability has dropped while that of EU firms has increased, perhaps because U.S. firms suppressed price increases leading up to the 2004 elections, or because they faced increasing price pressures from generic medicines and increased reimportation. This is consistent with Figure 1 that shows that real pharmaceutical prices were flat in the U.S. during 2003-2004, but increased in the EU.

These measures are standardized by size (total assets). How do U.S. and EU firms compare in terms of aggregate figures? Table 2 shows that U.S. firms have grown assets and R&D spending faster than EU firms. Between 1993 and 2004, EU firms' assets more than doubled but U.S. firms' more than quadrupled. U.S. R&D spending has grown 3.7 times over, while EU R&D has increased about 3.3 times.

Table 2

Comparison of Total Assets and R&D Spending for EU and U.S. Firms from 1993 to 2004

Year	Number of Firms		Total Assets (Billions \$)		R&D Spending (Billions \$)	
	U.S.	EU	U.S.	EU	U.S.	EU
1993	77	15	105.3	98.1	10.6	8.3
1994	93	19	139.6	127.5	11.5	10.2
1995	110	20	161.2	145.0	14.4	13.1
1996	120	24	173.2	175.0	16.2	14.5
1997	133	28	181.8	177.5	18.2	13.4
1998	143	30	211.8	168.2	22.0	14.7
1999	132	35	232.7	215.7	23.1	17.1
2000	112	38	246.6	216.7	24.2	19.7
2001	113	38	297.1	226.1	31.7	19.5
2002	112	37	333.6	237.2	33.3	23.6
2003	104	32	426.2	261.8	40.6	26.8
2004	96	30	467.7	255.3	39.6	27.4

The U.S. and EU samples change year-to-year as new public firms enter the industry and others liquidate or merge.⁷ To the extent that other sample firms purchase these firms, the totals remain reasonable measures of total assets and R&D spending. Of course, the geographic location of assets and R&D are not necessarily consistent with these figures if there has been a relative switch from EU to U.S. for EU firms or vice versa. We will consider this issue in the next section.

⁷ The Compustat Global Industrial/Commercial data used for this table contains some errors that we have corrected. The errors were contained in the EU firms' data, perhaps because Compustat's U.S. database has been available for many years (since 1950) and its foreign portion of the Global database is relatively new (since 1993). Figures for Aventis between 1999 and 2003 needed to be multiplied by 1000, as did AstraZeneca's figures for 1997. R&D figures for GlaxoSmithkline between 1993 and 1995 and Novo-Nordisk in 1993 were incorrect due to typographical errors. All of these were changed based upon figures found in the firms' annual reports. Finally, the very large merger between Sanofi and Aventis in 2004 posed a unique problem. Instead of Compustat figures, which reflected merger-related accounting, we simply used the firms' combined 2003 figures for the combined firm in 2004. This likely understates the true figures somewhat, but because the firm book a very large intangible asset to reflect the premium paid for the merger, the reported figures are large enough to cause the EU totals to be substantially overstated.

Another way to consider the effects of EU price regulation is to examine stock return performance for EU firms compared to U.S. firms. Doukas and Switzer (1992) show that stock prices respond favorably to R&D spending. If EU firms are not comparatively disadvantaged by price regulation, then EU and U.S. pharmaceutical stocks should perform comparably over time. Performance is measured by cumulative total and risk-adjusted returns between 1993 and 2004 for market-value-weighted portfolios of EU and U.S. stocks (for the same samples used in Tables 1 and 2). For each full year of data available for a firm, its annual return is computed using prices and dividends taken from Compustat's Global Issues database. All prices and dividends are translated into dollars using Compustat's Global Currency database. Then for each year, each EU firm's return is weighted by its equity market value divided by the total equity market value of all EU firms with returns in that year. These weighted returns are summed for each year, and then the weighted-average returns are cumulated over the 1993 to 2004 period. Cumulative total returns for the portfolio of U.S. firms are computed in the same way.

Because the risk of EU and U.S. pharmaceutical stocks could differ, differences in total returns could be due to risk differences. Therefore, we consider risk-adjusted returns as well. The following single factor market model is used to estimate the annual risk-adjusted returns for each firm.

$$R_{it} = \alpha_i + \beta_i R_{mt} + \varepsilon_{it} , \quad (1)$$

where R_{it} is firm i 's stock return in year t , R_{mt} is the market return in year t represented by the value-weighted Morgan Stanley Capital International World Index (dollar return),

α_i and β_i are ordinary least squares coefficients for firm i , and ε_{it} is the error term for firm i in year t .

Model 1 is estimated for each firm using its available annual returns. Then its risk-adjusted return ($RAR_{i,t}$) in year t is computed using estimates of α_i and $\varepsilon_{i,t}$ from (1) as;

$$RAR_{i,t} = \hat{\alpha}_i + \hat{\varepsilon}_{i,t}. \quad (2)$$

Like total returns, risk-adjusted returns are value-weighted and cumulated over 1993 to 2004 for portfolios of EU and U.S. firms' stocks, respectively. The cumulative total and risk adjusted returns series for EU and U.S. portfolios are plotted together in Figure 2.

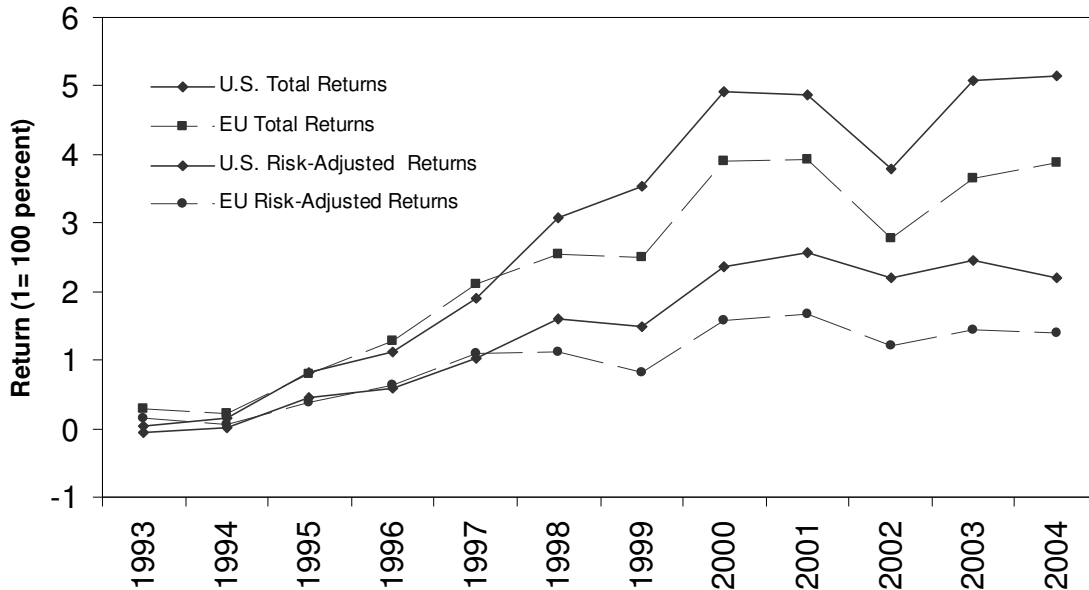


Fig. 2. Total Dollar-Denominated Returns and Risk-Adjusted Returns for Market-Value Weighted Portfolios of U.S. and EU Pharmaceutical Stocks for 1993-2004

Figure 2 helps illustrate the effects of price controls on pharmaceutical stock prices. Between 1993 and 1997, U.S. and EU pharmaceutical stocks performed comparably. This is consistent with the pattern in the price indexes, which was flat for both the U.S. and the EU. U.S. prices rise in 1998 and 1999, while EU prices remain flat. This is also when U.S. stocks start to outperform EU stocks on a total return and risk-adjusted return basis. U.S. stocks maintain or expand their performance lead up until 2004, when EU stocks narrow the gap. Note that 2004 is also when the EU price index increases substantially more than the U.S. index.

Looking back at Table 2, one can see a similar pattern in R&D spending, where U.S. firms substantially increase R&D spending compared to EU firms in 1998, but the reverse occurs in 2004. After computing the difference in the U.S. and EU price indexes, we related these figures to the differences between U.S. and EU stock returns. The correlation over 1993-2004 between the U.S.-EU price index differences and the total return (risk-adjusted) differences is 0.93 (0.94), highly statistically significant. The correlation between U.S.-EU pharmaceutical price change differences and U.S.-EU R&D intensity differences is 0.64, also statistically significant. U.S.-EU R&D intensity differences are also significantly related to U.S.-EU profitability differences (correlation is 0.82).

Although attributing causality is always difficult, these correlations support an association between pharmaceutical price control differences and R&D spending

differences. And these R&D spending differences appear to lead to stock return differences, consistent with Doukas and Switzer (1992) findings. Indeed, the levels of returns are high for both U.S. and EU pharmaceutical stock, perhaps because they both spend heavily on R&D. But when pharmaceutical prices expand faster for one geographic area, firms in that area tend to spend more on R&D, and their stocks benefit.

4. U.S.-EU R&D Growth Differences

A weakness of the Compustat Global data is that it includes only publicly reported data. Another problem is that firms report total R&D spending, not spending by geographic area. Finally, total R&D spending can include R&D spent by non-pharmaceutical divisions of the firm (although most produce primarily pharmaceuticals).

Two other data sources avoid these potential problems. The European Federation of Pharmaceutical Industries and Associations (EFPIA) has collected European R&D spending data from its members since 1986.⁸ The Pharmaceutical Research and Manufacturers of America (PhRMA) has collected U.S. R&D spending data from its members since 1970.

These two associations include most major pharmaceutical firms (both U.S. and EU firms), hence, their data provides a reasonable picture of pharmaceutical R&D spending in the U.S. and EU. They provide aggregate data only. For privacy reasons, they do not release firm-level data. The advantage of the data is that EFPIA's (PhRMA's) members report not only their total R&D, but also their EU-specific (U.S.-specific) R&D.

⁸ EFPIA member association include those in Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Netherlands, Norway, Portugal, Spain, Sweden, Switzerland, and U.K.

Furthermore, EFPIA translates R&D figures reported by its members from their domestic currencies into Euros. We convert the Euro figures to dollars.

Figure 3 illustrates the magnitude and the timing of changes in pharmaceutical R&D spending in Europe and the U.S. R&D spending in Europe exceeded U.S. spending by about 24 percent in 1986 (\$4790 vs \$3875), but by 2004, European spending trailed U.S. spending by about 15 percent (\$26725 vs. \$30644). U.S. R&D spending does not outgrow European spending in every year, however. For example, in 1994 and 1995, European R&D growth exceeds U.S. growth (perhaps due to the Clinton administration's proposed pharmaceutical price constraints).

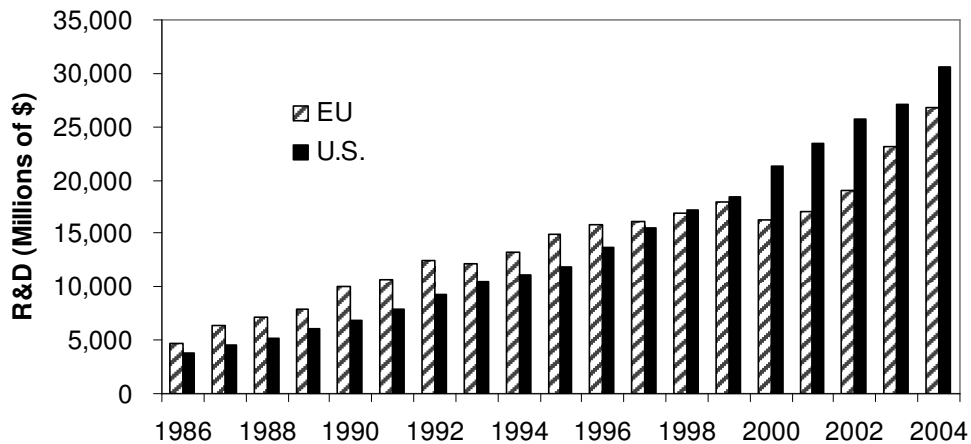


Fig. 3. EU and U.S. Pharmaceutical R&D Spending in Millions of Dollars for the Years from 1986 to 2004

Like Table 2, Figure 3 shows that EU R&D spending stalls in 1997 and 2001. U.S. R&D spending grows throughout the period including in 2004. Table 2 shows a decline in 2004 U.S. R&D spending. At least part of the explanation for the differences between figures in Table 2 and Figure 3 is that there are shifts in R&D spending from the EU to the U.S., or vice versa.

There is anecdotal evidence that EU firms have recently shifted some R&D spending from the EU to the U.S. Consider that in 1990, European firms spent 73 percent of their R&D in Europe and 26 percent in the U.S. By 2002, they spent 58 percent in Europe and 34 percent in the U.S.⁹ Major European firms have moved their research or operational headquarters to the U.S., including Pharmacia in 1995, Aventis in 1999, GlaxoSmithKline in 2000, and Novartis in 2002. Reasons given for these moves include growing U.S. sales compared to EU sales, and requirements that they perform clinical trials in the U.S., particularly FDA phase three trials. U.S.-based trials also establish relationships with top U.S. physicians who set prescription guidelines for other physicians.

Firms may be affected in different ways and at different times, but we argue that EU price regulations have had substantial cumulative effects. One case where public data is available illustrates the direct connection between regulation and EU R&D spending. Spain and France set a price for Bayer's second best-selling drug (Adalat) 40 percent below its price in England. When Bayer restricted supply to French and Spanish wholesalers who were reselling their supplies in England, the European Commission fined Bayer 3 million Euros in 1996, and ordered them to stop restricting supply. World-wide sales of Adalat, which had been growing strongly, subsequently fell by four (three)

⁹ EFPIA, "Year in Review 2001-2002."

percent in 1998 (1999), mostly due to French and Spanish wholesalers reselling Adalat at relatively low prices. As a consequence, Bayer cut its European R&D spending by one percent in 1998 and by 14 percent in 1999. Conversely, Bayer increased its U.S. R&D spending by eight percent in 1998 and by 31 percent in 1999.¹⁰ Bayer may have expected the U.S. legal system to better protect their rights to control product distribution.

Some U.S. government data on foreign firms' pharmaceutical R&D spending in the U.S. shows that their spending grew from \$6.2 billion in 1999 to \$7.9 billion in 2003. Conversely, U.S. firms foreign pharmaceutical R&D grew from only \$2.8 billion in 1999 to \$3.2 billion in 2002.¹¹ The R&D data are not broken down by country but the Bureau of Economic Analysis reports U.S. pharmaceutical assets held by foreign firms broken down by country. European nations accounted for between 80 and 90 percent of these assets during 1999-2003.

These data show that foreign firms do much more pharmaceutical R&D spending in the U.S. than U.S. firms do abroad. Furthermore, foreign firms' U.S. R&D is growing faster. Therefore, Table 2 shows a smaller difference between U.S. and EU R&D than Figure 3 because the table does not pick up the fact that EU firms spend a much larger portion of their R&D in the U.S. than U.S. firms spend in the EU.

One problem with comparing figures adjusted for exchange rates is that exchange rates can change significantly year-to-year, distorting the relative growth in R&D in

¹⁰ Figures taken from Bayer annual financial reports 1997-2001.

¹¹ The data on foreign firms' U.S. pharmaceutical R&D spending comes from the Bureau of Economic Analysis. See "Selected Data by Industry" under Foreign Direct Investment in the U.S.: Financial and Operating Data for U.S. Affiliates of Foreign Multinational Companies (www.bea.gov/bea/di/di1fdiop.htm). The data on assets can be found at the same place under "Assets by Industry and Country. These data are available starting in 1999. The data on U.S. firms' foreign pharmaceutical R&D spending comes from tables titled "Company R&D Performed Outside the United States by Industry" at www.nsf.gov/statistics/iris. Data for 2002 is the latest available.

particular years. Perhaps a better way to compare the relative progress of U.S. and European R&D spending is to construct real growth rates for each series in dollars and Euros, respectively, and ignore exchange rates. Over a long period, relative changes in exchange rates will appear in relative inflation rates so that adjusting nominal R&D growth rates for domestic inflation provides smoother, more comparable series.

Figure 4 shows the smoothed time paths of R&D growth, making trends and average differences clearer. It plots the average annual compound real R&D spending growth rates for the U.S. and Europe. The growth rates are based on the same PhRMA and EFPIA data, except that EU figures remain in Euros. Real growth is nominal growth deflated by the CPI percent change for the same year. Each year's observation is the average annual real R&D growth for the years up to and including that year. The figure highlights two significant features of the data. First, both U.S. and EU R&D spending growth rates are trending down. The average real growth rates for the first five years of the period compared to the last five years were 9.9% versus 7.6% for the U.S., and 6.6% versus 2.8% for Europe. This could be due to the effects of increasing political pressures in the U.S. and regulatory pressures in the EU.

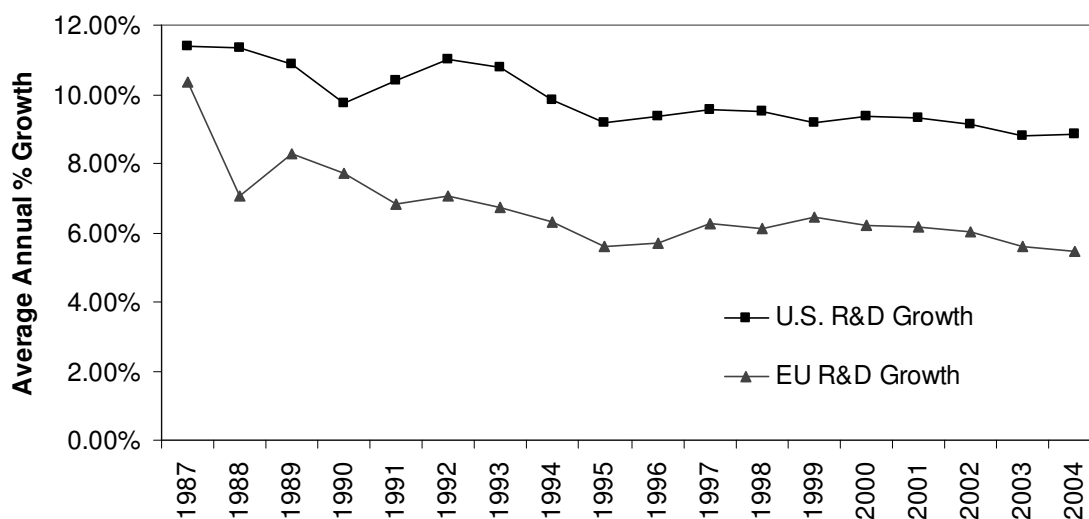


Fig. 4. Average Annual Real Growth in U.S. and EU Pharmaceutical R&D Spending between 1987 and 2004

Second, U.S. growth consistently exceeds European growth by an average of 3.4 percentage points per year over the full 1987 to 2004 period. Over long periods of time such as this, there can be considerable cumulative effects of spending differences on the number of new pharmaceutical products developed in the EU versus the U. S. Indeed, EFPIA reports that between 1987 and 1991, European firms introduced 101 new medicines while U.S. firms introduced 54. But between 2000 and 2004, European firms introduced 57 new medicines while U.S. firms introduced 70.¹²

¹² See EFPIA “The Pharmaceutical Industry in Figures,” 2005, and “Year in Review 2001-2002,” 2002.

5. Linking Real Pharmaceutical Price Inflation to Firms' R&D Spending

We wish to test the cross-sectional relation between EU price regulations and R&D spending at the firm-level. Real pharmaceutical prices are used as a proxy for the effects of price regulations and political pressure in the U.S. and EU over time. Giaccotto, Santere, and Vernon (2005) find a statistically significant positive relation between U.S. industry-level R&D spending and real U.S. pharmaceutical prices. We implement our test using a two-stage process. In the first stage, we estimate the following regression for each firm in our samples of U.S. and EU firms.

$$(\text{Sales/Assets})_{i,t} = b_0 + b_{i,1}(\text{U.S. Price index})_t + b_{i,2}(\text{EU Price Index})_t + \varepsilon_{i,t} , \quad (3)$$

where $(\text{Sales/Assets})_{i,t}$ is the ratio of sales to total assets for firm i in year t , $(\text{U.S. Price index})_t$ and $(\text{EU Price Index})_t$ are the U.S. and EU real pharmaceutical price indexes in year t , respectively, $\varepsilon_{i,t}$ is an error term for firm i in year t , and b_0 , b_1 , and b_2 are ordinary least squares regression coefficients.

The regression coefficients $b_{i,1}$ and $b_{i,2}$ are used to measure the sensitivity of a firm's sales to U.S. and EU price indexes, respectively. Firm sales are standardized by assets to account for firm size and currency differences. All else equal, faster real prices increases should increase sales faster than assets, assuming that real pharmaceutical price changes do not affect the real cost of production facilities. We expect firms whose sales are more sensitive to U.S. (EU) pharmaceutical prices to spend more (less) on R&D. To test this hypothesis, we use the following regression.

$$(\text{mean R\&D/Assets})_i = \beta_0 + \beta_1(\hat{b}_{i,1}) + \beta_2(\hat{b}_{i,2}) + \varepsilon_i, \quad (4)$$

where $(\text{mean R\&D/Assets})_i$ is the mean of firm i 's ratio of R&D spending to total assets over the years for which it has Compustat data between 1993 to 2004, $\hat{b}_{i,1}$ and $\hat{b}_{i,2}$ are coefficient estimates from (3) that measure firm i 's sales sensitivity to U.S. and EU price indexes, respectively, β_0 , β_1 , and β_2 are coefficients, and ε_i is an error term. The hypothesis implies that $\beta_1 > 0$ and $\beta_2 < 0$. That is, the more sensitive a firm's sales are to the U.S. (EU) price index, the greater its R&D spending.¹³

Table 3 reports the regression results. Note that both U.S. and EU firms are pooled for this analysis. As predicted, $\hat{\beta}_1 > 0$ and $\hat{\beta}_2 < 0$. These estimates support a significant positive (negative) relation between a firm's sales sensitivity to U.S. (EU) real prices and mean R&D spending intensity.

¹³ Because the independent variables ($\hat{b}_{i,1}$ and $\hat{b}_{i,2}$) are measured with error, the estimates of β_1 and β_2 could be biased. Greene (1990) shows that when one independent variable is measured with error, its estimate is biased toward zero, but when more than one independent variable is measured with error, the bias depends on a number of parameters. To the extent that the estimates are biased toward zero, the tests for statistical significance are conservative.

Table 3

The Relation between Firm R&D Spending and Firm Sales Sensitivity to U.S. and EU Real Pharmaceutical Prices

Dependent Variable	Intercept	U.S. Price Sensitivity β_1	EU Price Sensitivity β_2	R-Squared	F-Statistic
Mean	0.24	0.12**	-0.10*	0.08	7.74*
R&D/Assets	(13.40)	(2.02)	(3.92)		

*(**) Statistically significant at the 1% (5%) level. Sample size is 181 firms.

6. EU Price Regulation and the Long-term Costs of Slower R&D Spending

In this section we estimate the potential costs of European-style pharmaceutical price regulations in terms of foregone new medicines and research jobs. We rely on the R&D growth figures observed in Figure 4. Both U.S. and EU R&D spending are growing slower, with EU spending growing comparatively slower than U.S. spending. Consequently, the total of U.S. and EU new medicines introduced fell from 155 between 1987 and 1991, to 127 between 2000 and 2004. This illustrates that while EU firms are most affected by EU regulations, U.S. firms are also affected. U.S. political pressure probably affects both groups as well. Indeed, six of the 21 firms that agreed to constrain their prices in response to Clinton's proposed Health Security Act were EU firms.

Vernon (2005) provides a detailed quasi-structural model and robust empirical model of pharmaceutical R&D investment that shows that European-like pharmaceutical regulation in the U.S. would lead to a one-time R&D decline of between 23.4 and 32.7

percent. Giaccotto, Santerre, and Vernon (2005) found similar one-time effects using a very different estimation method. But rather than a one-time decline, R&D spending would likely grow slower as stricter regulations are adopted over time. Even at low prices, some relatively-promising new R&D projects and late-stage projects would continue to be funded.

We analyze the impact of R&D growth declines with three related models. The models are used to compute the present value of R&D expenditures under different R&D growth assumptions. They provide estimates of cumulative effects on R&D spending over various time periods. The first is used to model an R&D growth drop from its current fixed long-term rate, to a new lower long-term rate. The model is:

$$PVRD_t = \frac{RD_{t+1}}{(k - g)}, \quad (5)$$

where RD_{t+1} is pharmaceutical R&D spending in year t+1, $PVRD_t$ is the present value of future pharmaceutical R&D spending, k is the discount rate associated with R&D spending flows, and g is the constant future growth of R&D spending.

The second model is used to evaluate and compare R&D spending over shorter periods of time. The model is:

$$PVRD_t = \frac{RD_{t+1} \left[1 - \frac{(1 + g_s)^n}{(1 + k)^n} \right]}{(k - g_s)}, \quad (6)$$

where g_s is the short-term growth in R&D spending from year t through year n ,

The third model covers a long time period but assumes that growth falls to a moderate rate for n years and then falls again to a new long-term rate. The model is:

$$PVRD_t = \frac{RD_{t+1} \left[1 - \frac{(1+g_s)^n}{(1+k)^n} \right]}{(k-g_s)} + \frac{RD_{n+t+1}}{(k-g_L)(1+k)^n}, \quad (7)$$

where RD_{n+t+1} is R&D spending in year $n+t+1$, and g_L is the long-term growth in R&D spending starting in year $n+t+1$ and continuing forever.

We use the real growth rates observed in the data above for these models. The Appendix shows how Vernon's (2005) one-time R&D spending decline relates to R&D growth declines. Estimates of the real discount rate (k) for pharmaceutical industry cash flows are found in DiMasi, Hansen, and Grabowski (2003), Myers and Shyam-Sunder (1996), and Grabowski and Vernon (1990) and range from nine to 11 percent. We will use a ten percent rate in the following analysis.

We estimate the costs of slower real R&D spending growth in terms of the present value of real R&D spending foregone, and then translate real R&D foregone into fewer new medicines and scientists employed. To translate real R&D spending foregone into new medicines foregone, we use two estimates of the present value of R&D cost per new medicine. The first estimate reported in DiMasi, Hansen, Grabowski, and Lasagna (1991) of about \$114 million in 1987 dollars (\$108.6 in 1985 dollars) is used to estimate new medicines foregone by the EU during our sample period of 1986-2004. The second estimate reported in DiMasi, Hansen, and Grabowski (2003) of about \$403 million in

2000 dollars (\$439 million in 2004 dollars) is used to estimate new medicines foregone by the EU and the U.S. for all future years.

To translate real R&D spending foregone into pharmaceutical scientist jobs foregone, we use National Science Foundation figures that show R&D expenditures per R&D employee in the Pharmaceuticals and Medicine Manufacturing industry (NAICS 3254) was \$225,693 in 2001 (in constant 1996 dollars).¹⁴ The Bureau of Labor Statistics reports that medical scientists in the industry earned about \$77,000 in wages (\$36.92 per hour median wage).¹⁵ Given that other compensation is likely to be at least half the cost of wages, then total employee compensation is about half of the \$225,693 spent on R&D per R&D employee. We use \$112,846 (in 1996 dollars) in the computations below.¹⁶

Table 4 presents estimated costs of EU-type regulation under three different scenarios. First are the costs to the EU of price regulation already incurred during the 1986-2004 period. Model (6) is used in this case. The second and third are the prospective costs to the EU and the U.S. of price regulation in the future. Models (5) and (7) are used to estimate prospective costs for the EU and the U.S., respectively

¹⁴ See Industrial R&D Employment in the United States and in U.S. Multinational Corporations, National Science Foundation, 2004.

¹⁵ See Bureau of Labor Statistics, Pharmaceutical and Medical Manufacturing (NAICS 3254), 2004, (www.bls.gov/oco/cg/pdf/cgs009.pdf).

¹⁶ Data on the distribution of R&D expenditures in the pharmaceutical and biotechnology industries across labor and non-labor inputs is not typically available in firms' financial statements. We searched the financial statements filed on the SEC's EDGAR database for those that discussed their labor inputs, and labor was mentioned as at least a majority of R&D expenses. We conducted a limited analysis of "pure play" biotechnology firms with R&D expenditure and labor expense data listed on Compustat. These firms had little or no revenue from marketed products so they were solely research firms. Under reasonable assumptions about the distribution of labor expense between R&D and non-R&D employees, labor represents close to 90 percent of their R&D expenses.

Table 4

Estimated Costs of EU-Type Pharmaceutical Price Regulation in Terms of Foregone R&D Spending, Fewer New Medicines, and Fewer Scientists Employed

Scenario	Foregone R&D Spending	Foregone New Medicines	Foregone R&D Job Years*
(1) Costs Incurred by the EU during 1986-2004 due to real R&D growth at 5.4% instead of 6.6%	\$4.96 Billion (1985 dollars)	46	31,925
(2) Prospective Costs to EU from 2004 onward due to real R&D growth at 2.8% instead of 5.4%	\$280.78 Billion (2004 dollars)	526	1,035,953
(3) Prospective Costs to U.S. from 2004 onward due to real R&D growth at 5.4% for 18 years followed by 2.8% thereafter instead of 6.6% throughout	\$427.40 Billion (2004 dollars)	974	1,578,081

*Uses CPI annual inflation rates to adjust \$112,846 (1996 dollars) compensation cost per research employee to the appropriate year.

For the first scenario, foregone European R&D spending is estimated by comparing *PVRD* calculated using Europe's actual 1987-2004 annual real R&D growth (5.4%), to *PVRD* assuming that EU growth of 6.6% between 1987 and 1991 could have been maintained if regulations were more comparable to the U.S. Note that U.S. annual real R&D growth during the period averaged considerably more; about 8.8 percent. Some of that growth probably reflects a shift of R&D spending by EU firms from the EU to the

U.S. Given this, a 6.6 percent EU growth under U.S.-type pricing condition seems reasonable.

The costs for this scenario are \$4.96 billion EU R&D foregone during 1986-2004, which would have produced 46 new medicines and 31,925 job years. This is equivalent to 1680 EU research jobs for the 19 years. These figures are reasonable in light of the fact that EU firms actually introduced 101 new medicines between 1987 and 1991, but 44 less between 2000 and 2004. Of course, one could argue that some of the EU R&D spending foregone was partly reallocated and spent in the U.S. Indeed, for the same comparison periods, the U.S. experienced an increase of 16 new products. Assuming that these were derived from R&D spending transferred from Europe still leaves 28 foregone medicines on net for the five years. Extrapolating over the 19 year period, this is equivalent to about 106 foregone new medicines. Hence 46 new medicines foregone could be an underestimate.

The second scenario estimates future long-term foregone European R&D spending by comparing *PVRD* calculated using Europe's most recent five-year (2000-2004) average annual real R&D growth (2.8%), to *PVRD* assuming average EU growth over 1986-2004 (5.4%). Costs for this scenario, of course, are much larger because the growth difference is larger and all future years are covered. Forgone future R&D is estimated at \$280.78 billion in 2004 dollars. This is equivalent to 526 new medicines foregone and 1,035,953 lost job years.

The third scenario estimates future long-term foregone U.S. R&D spending. Assuming that the U.S. adopts EU-type price regulation gradually over the 19 years starting in 2005, we project that U.S. real growth will be comparable to the EU's 5.4

percent average real growth rate during 1986-2004. After 19 years, the same long-term real growth rate assumed for the EU (2.8%) is adopted for the U.S. *PVRD* based upon this two-stage growth decline is compared to *PVRD* estimated using a constant 6.6 percent future growth rate. Forgone future R&D is estimated at \$427.40 billion in 2004 dollars. This is equivalent to 974 new medicines foregone and 1,578,081 lost job years.

Costs estimated in scenarios two and three may seem large, but they represent annual R&D growth rate declines of only a few percentage points at most. The gradual accumulation of costs may not produce the political response that a large one-time drop of 20-30 percent would cause. But the growing gap between EU and U.S. pharmaceutical R&D, and the movement of R&D facilities to the U.S. by EU firms, should be a signal to EU policymakers that low pharmaceutical prices through regulation has its costs.

7. Conclusion

This paper illustrates how the gap between U.S. and European pharmaceutical R&D spending has changed over the 19 years from 1986 through 2004. Europe outspent the U.S. by about 24 percent in 1986, but by 2004, the U.S. was outspending Europe by about 15 percent. From 2000 to 2004, U.S. spending grew at a 6.6% rate compared to 2.8% for Europe. If this growth difference persists for another five years, U.S. R&D spending will exceed Europe's by 37%.

The implicit cost in terms of new medicines foregone is large. If European R&D spending had grown at 6.6% over the last 19 years instead of its actual 5.4% rate, about 46 new medicines would have been produced. R&D growth has trended down for both

the U.S. and Europe, but the gap in growth rates between the U.S. and Europe has remained quite stable at about 3.4 percent. The general downward trend could reflect weaker real price increases in the U.S. since 1992 and no real price increase in Europe throughout. Threatened or actual pharmaceutical price regulation could account for this weaker price growth and, consequently, weaker R&D growth.

Slower R&D growth as a consequence of price regulation and reimportation may be politically acceptable because current consumer benefit, but we show that the cost to future generations is substantial. European-type policies adopted in the U.S. could lead to 974 fewer new medicines and 1,578,081 lost job years in the future. Because new medicines improve health and extend lives (see Lichtenberg 1996, 2003), these policies essentially trade off the health and employment opportunities of future generations for cost savings for current pharmaceutical consumers.

Appendix

Vernon's (2005) one-time decline of between 23.4 and 32.7 percent in R&D spending due to European-like regulation might seem large, but model (5) can be used to show that a relatively small R&D growth rate decline can produce the same result. To see this, use (5) assuming a one-time drop in R&D spending of α and equate it to (5) assuming a decrease in R&D spending growth of λ .

$$\frac{(1-\alpha)RD_{t+1}}{(k-g)} = \frac{RD_{t+1}}{(k-(1-\lambda)g)} \quad (1A)$$

This implies that

$$\lambda = \frac{\alpha(k-g)}{(1-\alpha)g} \quad (2A)$$

We compute λ from (2A) using expected future U.S. R&D real growth rates between 8% and 6%.

Table 1A

Proportional Change (λ) in Real U.S. R&D Growth Rate Equivalent to a One-time 30 Percent Decrease in R&D Spending Due to European-like Price Regulation

Real Discount Rate	Expected Future U.S. R&D Pharmaceutical Real Growth Rate		
	6%	7%	8%
9%	0.21	0.12	0.05
10%	0.29	0.18	0.11
11%	0.36	0.24	0.16

Assuming a one-time R&D spending decrease of 30%, Table 1A shows that the equivalent change in R&D spending growth is proportionately smaller in all cases except for one. The average value of λ is 18 percent. For example, this means that if expected real R&D spending growth is 7% and the real discount rate is 10%, then European-like price regulation would decrease growth from 7% to 5.7%. Given that European real R&D spending growth fell from 6.6% to 2.8% during 1987 to 2004, Vernon's predicted one-time decrease for U.S. spending could be an underestimate.

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