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GENERIC UTILIZATION RATES, REAL PHARMACEUTICAL PRICES, AND RESEARCH AND DEVELOPMENT EXPENDITURES

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ABSTRACT

Generic utilization rates have risen substantially since the enactment of The Drug Price Competition and Patent Term Restoration Act (Hatch-Waxman) in 1984. In the year Hatch-Waxman was enacted, generic utilization rates were 19 percent; in contrast, today, the generic utilization rate is approximately 70 percent. Striking a balance between access to existing medicines and access to yet-to-be-discovered (and developed) drugs, through research incentives, was the principal objective of this landmark legislation. However, given the current rate of generic utilization, it seems plausible, if not likely, that any balance achieved by the 1984 Act has since shifted away from research incentives and towards improved access, ceteris paribus. Among other factors, recent mandatory substitution laws in most states have driven up generic utilization rates. In the current paper, we employ semi-annual data from 1992 to 2008 to examine the link between generic utilization rates and real U.S. prescription drug prices. This link is important because previous research has identified a causal relationship between real drug prices in the U.S. and industry-level R&D investment intensity. We identify a statistically significant, positive relationship between generic utilization rates in the U.S. and real U.S. prescription drug prices. Specifically, we estimate an elasticity of real drug prices to generic utilization rates of -0.15. This finding, when coupled with previous empirical work on the determinants of pharmaceutical R&D intensity, suggests an elasticity of R&D to generic utilization rates of about 0.090. While the magnitude of this elasticity is modest, as theory would predict—the effect of greater generic erosion of brand sales at patent expiration is heavily discounted due to the long time horizon to generic erosion when an R&D project is in clinical development. However, because there has been a very substantial increase in generic utilization rates since 1984, the impact on R&D is nevertheless quite large. We explore this and other issues in the current paper.

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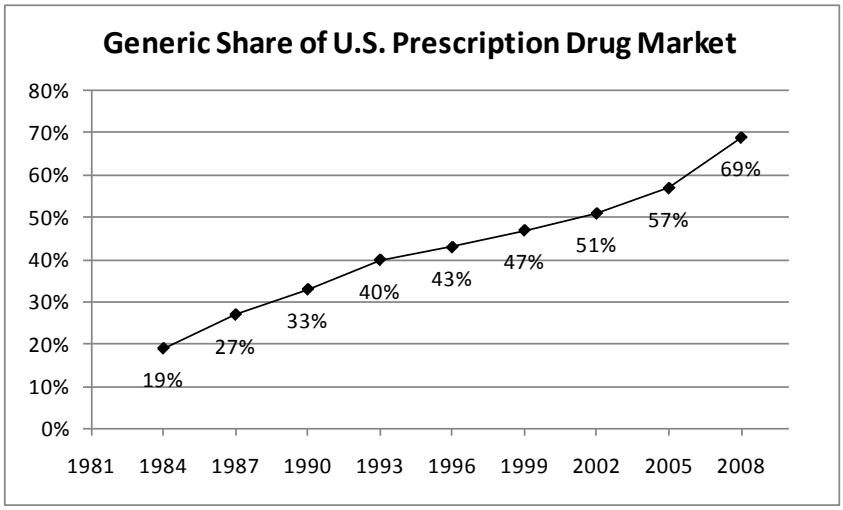
I. Introduction

Since the enactment of the Drug Price Competition and Patent Term Restoration Act of 1984 (also known as the Hatch-Waxman Act), the share of all U.S. prescriptions that are filled with generic drugs has increased substantially: from 19 percent in 1984 to 69 percent in 2008 (GPhA, 2009; PhRMA 2007 Annual Report; IMS Health Reports Press Release, March 12, 2008). See figure 1 below. Hatch-Waxman greatly facilitated generic entry by significantly lowering the associated costs of bringing a generic drug to market, and continues to do so (Grabowski and Vernon, 1986; 1992). Instead of replicating the same long, costly, and risky clinical trials already undertaken by the brand manufacturer to gain FDA approval under a New Drug Application (NDA), generic firms need only show bioequivalence with the off-patent drug as part of an Abbreviated New Drug Application (ANDA). The cost savings to generic manufacturers have been substantial. The time from discovery to market launch for a new brand drug has been recently estimated between ten and 15 years and costs in excess of $1 billion (DiMasi, Hansen, and Grabowski, 2003; Vernon, Golec, and DiMasi, 2010). In contrast, it costs only $1-2 million for a generic manufacturer to demonstrate bioequivalence to a branded drug (Saha, Grabowski, and Birnbaum, et al., 2006). As one would expect, the increased ease of generic approvals has been associated with significant growth in the generic pharmaceutical industry. Over the past two decades, the generic industry's revenues have grown from $1 billion to $63 billion.

Figure 1: Annual Trend in Generic Utilization Rate in U.S. After Hatch-Waxman[1]



For branded manufacturers, while Hatch-Waxman also contains provisions for patent-term restoration (e.g., extending the patent length to account for the time it takes the FDA to review and approve a new branded drug), there has also been a sharp rise in clinical development costs (DiMasi, Hansen, and Grabowski, 2003; Grabowski, 2003). This increase in costs results from a greater number of clinical trials, which are larger and more complex than they were in 1984, to compete effectively and to meet FDA requirements. For example, data compiled by the Tuft's Center for the Study of Drug Development (DiMasi, 2003) estimates that the mean number of subjects in clinical trials per NDA has risen more than four-fold, from 1,312 in 1984 to 5,621 in 2000. Also, clinical trial complexity is estimated to have increased by more than 40 percent between 1992 and 2000 (DataEdge, 2002). As a result, much of Hatch-Waxman's innovation incentives via patent restoration, balanced with enhanced generic competition, have

[1] Source: AARP Public Policy Institute: assets.aarp.org/rgcenter/health/i16_generics.pdf

arguably been eroded, and the balance originally struck by the 1984 Act has thus likely shifted as expected returns to R&D have declined, ceteris paribus. See, for example, Cook (1998).[2]

The concomitant effect on drug prices and branded drug revenues has also been striking. A very recent study found, for example, that in the case of a large brand product, generic entry and price competition will come swiftly (it may take only few years for a generic pharmaceutical to be ready for product launch); moreover, in cases where there are between 10 and 20 generic competitors entering the market, generic prices can be driven down to marginal production cost within a few months (Saha, Grabowski, Birnbaum, et al, 2006). One significant cause of this may be the dramatic increase in the level of generic utilization (as shown in figure 1 it has increased from 19 percent to 69 percent). For example, once Pfizer's Lipitor (generic name atorvastatin) goes off patent, the company could lose close to $6 billion annually in revenues from generic entry and competition.[3]

During much of the R&D phase of drug development, patent expiration is many years off; thus, the price erosion from any generic entry is discounted over many years. Nevertheless, the magnitude of the increase in generic utilization and the associated impact on real pharmaceutical prices is not trivial. This is particularly true for the more costly later-stage R&D projects and Phase IV research because generic entry is much closer on the horizon. Furthermore, for patented products brought in to compete against other brands in the same therapeutic drug class, they too, will face a shorter period of time on the market before generic entry into the class.

[2] Cook (1998), p. 50 ("CBO's analysis has found that the patent extensions available under the Hatch-Waxman Act were not sufficient to fully preserve the returns from marketing new brand-name drugs.")
[3] Lipitor sales in 2008 are reported to be $5.9 billion in the US. See http://www.drugs.com/top200.html

Generic entry can increase generic utilization in different ways. Generic utilization is a general measure of the use of generics and their prevalence in the market. It can increase either because of higher generic penetration (i.e., a greater percentage of drugs for which there is a generic version available) or because generics capture greater shares of markets that have already experienced generic entry. Higher generic penetration in the U.S. was reported in a Congressional Budget Office (CBO) study in 1998,[4] and more recently by Aitken, Berndt, and Cutler (2009).[5] In addition to increasing the frequency of any given brand facing generic competition, enhanced generic entry can increase the intensity of generic competition by expanding the number of generic competitors. Research by Reiffen and Ward (2005) and Saha, Grabowski, Birnbaum et al. (2006) helps illuminate the effect of increasing the number of generic entrants on generic market share and prices. Saha, Grabowski, Birnbaum, et al. (2006), for example, report that the generic market share was about 79 percent where there were 20 or more suppliers in the first year, as opposed to 47 percent where there were only a few.[6]

More generally, factors that enhance generic competition can lead to increases in generic utilization and an accompanying reduction in the expected profitability of existing and future R&D projects for a new branded product. In addition to the reduced costs to gain FDA approval, we note that generic utilization can also increase as a result of state legislative efforts favoring generics (or even requiring them in some instances). In general, the expected returns for a prospective new branded product will decrease if generic competition is either more likely or

[4] See, e.g., Cook 1998, at p. xii ("Even more important, the act increased the proportion of brand-name drugs that face generic competition once their patents expire. In 1983, only 35 percent of the top-selling drugs with expired patents (excluding antibiotics and drugs approved before 1962) had generic versions available. Today, nearly all do.").

[5] Aitken et al. (2009) at p. w156 (noting that the generic penetration rate increased from 77.3 percent in 2003 to 86.4 percent in 2007).

[6] Saha et al (2006), pp. 15–38 ("The average market share a year after the first generic entry for compounds with at least 20 suppliers is 79 percent, while this share is only 47 percent for compounds with two or fewer generics.").

more intense, as either effect tends to decrease expected future revenues. Of course, a branded firm may be able to mitigate these effects to a modest extent using an authorized generic to compete for a share of the generic market revenues. According to the Federal Trade Commission's (FTC) interim report on authorized generics, an authorized generic may expect to capture roughly half the generic market revenues when competing against a single ANDA generic.[7] However, the authorized generics' price (and, thus, its revenues) will typically be discounted significantly relative to the brand.

Scherer (2001) found a persistent relationship between pharmaceutical gross margins and R&D expenditures. More recently, Giaccotto, Santerre, and Vernon (2005) found that lagged real U.S. pharmaceutical prices are an important determinant of industry-level R&D investment intensity (R&D expenditures as a percent of pharmaceutical sales revenues). This was argued to be the case because real pharmaceutical prices capture expectations of future prices, the degree of favorable overall market conditions, and profitability, as well as serving as a proxy for internally-generated cash flows. Since Grabowski's seminal paper on the determinants of industrial research and development (Grabowski, 1968), numerous subsequent studies have found a similar, and largely consistent, positive relationship between internally-generated cash flows and pharmaceutical R&D intensity (Grabowski and Vernon, 1981, 2000; Scherer, 1996; Vernon, 2005; Vernon, Golec, Lutter, et al, 2009; Golec, Hegde, and Vernon, 2010). Capital market imperfections result in a divergence between the cost of capital for internal funds and the cost of capital for external funds (debt and equity), with the latter being more costly.

[7] U.S. Federal Trade Commission (2009) "Authorized Generics: An Interim Report," p. 3 ("Revenues of a sole ANDA generic company during the180-day exclusivity period drop substantially with AG entry, with estimates of the average decline ranging from 47 percent to 51 percent.")

It follows, therefore, that increased generic utilization in the U.S. will affect real pharmaceutical prices in the U.S., and based on the discussion above, also R&D investment intensity. However, due to the construction of the real drug price index, as discussed more fully later, there is an empirical question as to the magnitude of the effect that generic utilization will have on the price index. We seek to answer this question in the current paper. We do this by estimating the relationship between generic utilization rates in the U.S. and real pharmaceutical prices, also in the U.S., and then mapping this mechanical relationship into the model of pharmaceutical R&D investment intensity estimated in Giaccotto, Santerre, and Vernon (2005). Giaccotto, Santerre, and Vernon estimated an elasticity of pharmaceutical R&D intensity to real U.S. pharmaceutical prices of 0.583, implying that for every 10 percent increase (decrease) in real pharmaceutical prices in the U.S., R&D intensity increases (decreases) by 5.83 percent. This is consistent with a similar elasticity estimate by Scherer (1996) of 0.61. By combining our findings on the impact of generic utilization rates on real U.S. pharmaceutical prices, with the aforementioned elasticity of R&D intensity to real U.S. pharmaceutical prices, we can measure the relationship between R&D intensity and generic utilization rates, the principal goal of our paper.

The rest of our paper will proceed as follows. Section II will introduce the theoretical model and discuss how generic utilization rates erode incentives for brand manufacturers. Section III will describe and discuss our data. Section IV will present our empirical results and discuss their implications. This section will also map our empirical findings on the link between generic utilization rates and real U.S. drug prices into the former's impact on R&D investment intensity. Section IV will conclude and offer suggestions for future research.

II. Theoretical Model of R&D Investment and Generic Drug Utilization Rates

To demonstrate the effect that increased generic utilization rates in the U.S. can have on the incentives to invest in pharmaceutical R&D we present a simple model in which firms make their R&D project investment decisions using the expected net present value (NPV) criterion and an R&D project's internal rate of return (IRR).

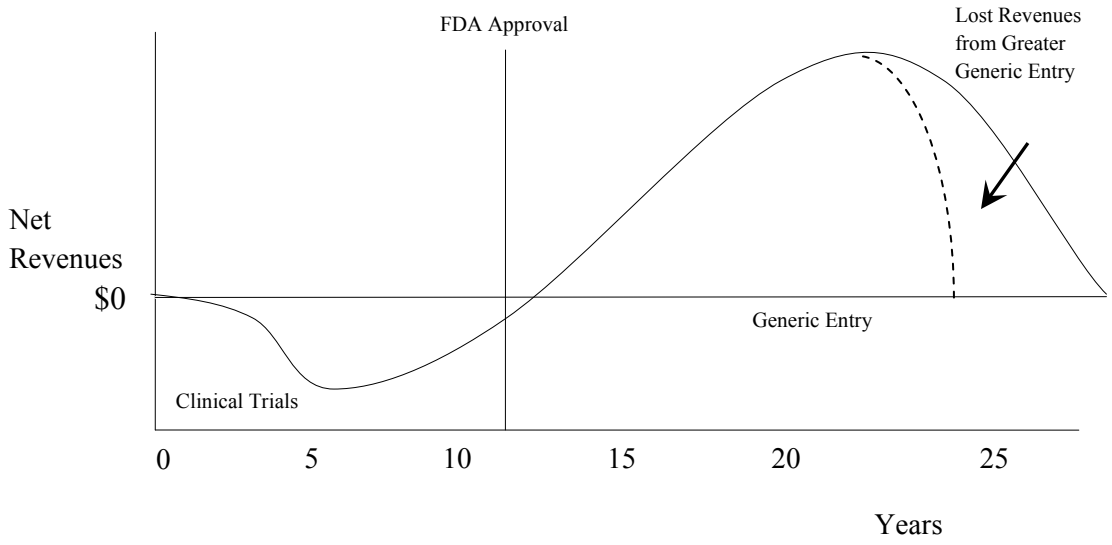
While increasing generic utilization rates can affect R&D project investment decisions at all stages in development, we focus our attention on later-stage R&D investment decisions, when generic competition will have the greatest affect on a project's expected NPV. Firms make development decisions by estimating expected net cash flows (C_t), which are after-tax, expected net revenues for the years a drug is expected to be on the market and after-tax, R&D-related, cash flows during the R&D project's developmental (and approval) stages. Thus, we can represent the expected NPV of an R&D project as follows:

$$E(NPV_0) = \sum_{t=0}^{T} \frac{E(C_t)}{(1+r)^t} = E(C_0) + \frac{E(C_1)}{(1+r)^1} + \frac{E(C_2)}{(1+r)^2} + \frac{E(C_3)}{(1+r)^3} + \ldots + \frac{E(C_T)}{(1+r)^T} \qquad (1)$$

In equation (1), r is an R&D project's cost of capital (assumed to be constant for expositional convenience) and T is the last year for which the R&D project, at this point a marketed product, is expected to generate cash flows. The effect of increased generic utilization rates on firm profits and cash flows is theoretically unambiguous. The magnitude of this effect, however, depends on numerous factors, such as the length of time until patent expiration (for the developmental drug or any same-therapeutic-class drug that faces patent expiration at an earlier date) or the degree of substitutability and the date of patent expiration for products in other therapeutic classes, as well as how the cost of financing R&D is affected by the availability and

level of internal funds. Figure 2 illustrates how present value revenues decline with higher generic utilization rates.

Figure 2: The Effect of Greater Generic Entry on Expected Cash Flows



Increased generic utilization rates (GURs) clearly have an impact on an expected project's NPV; however, the extent to which they have an impact is an empirical question. One thing is certain, since the enactment of the Hatch-Waxman Act in 1984, and the passage of legislation encouraging and mandating generic substitution, generic utilization rates have climbed very significantly: from 19 percent in 1984 to 69 percent in today's environment. Thus, the rate of return that a firm can expect to earn on its investors' capital for its R&D projects has fallen, ceteris paribus. This reduces a firm's profit-maximizing, or equilibrium, level of R&D investment. We illustrate this below in Figure 3, where the cross-hatched boxes reflect the difference between a project's internal rate of return in a market environment with a high generic

utilization rate (High GUR) and low generic utilization rate (Low GUR), holding all other factors constant, of course.

Figure 3: Equilibrium R&D Investment in the Presence of High and Low GURs

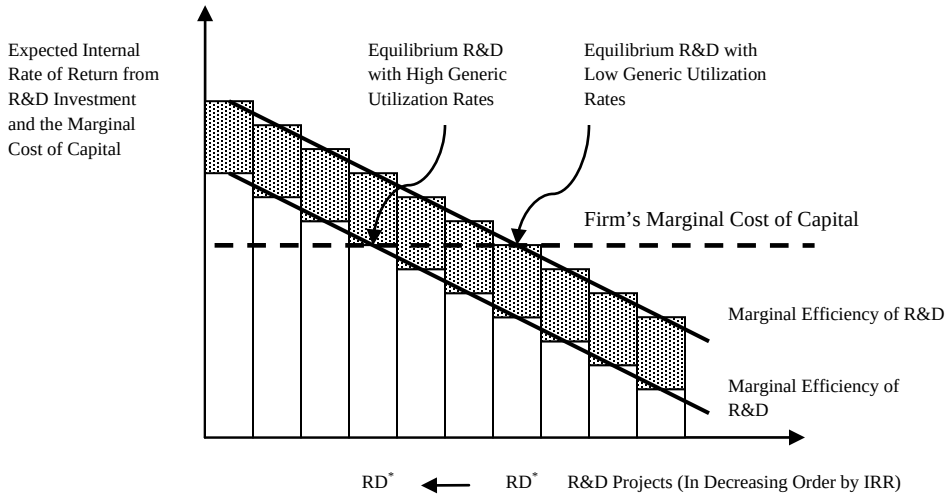


Figure 3 depicts two different marginal efficiencies of R&D: one in the presence of low generic utilization rates (the higher schedule) and one in the presence of high generic utilization rates (the lower schedule). These schedules are derived by arranging potential R&D investment projects in a decreasing order with respect to each project's expected internal rate of return. Firms will undertake the high return projects first, and continue to undertake additional investment projects, so long as the expected rate of return from the next project exceeds the firm's marginal cost of capital. This is the classic investment supply and demand framework.

Increasing generic utilization rates shifts the marginal internal rate of return schedule down, and fewer R&D projects meet the E(NPV) > 0 investment criterion, of earning an expected rate of return in excess of the cost of capital associated with the R&D project. Investors

will not supply capital to fund those marginal projects whose internal rates of return fall below their required returns, and for internally-financed projects, the expected rate of return falls below the project's opportunity cost of capital. Finally, figures 2 and 3 exclude the effects that internal cash flows have on capital supply to the firm. Capital market imperfections, perhaps due to transactions costs, tax advantages, asymmetric information, agency costs, or financial distress, may impart a cost advantage to financing R&D projects with internal cash flows instead of raising new capital from investors. Theoretical and empirical studies show that cash flows exert a positive influence on the level of firm investment spending (Malmendier and Tate 2005; Fazzari, Hubbard, and Petersen 1988; Hall 1992; Hubbard 1998; Grabowski, 1968, Grabowski and Vernon, 1981, 2000; Scherer 2001; Vernon 2005; Giaccotto, Santerre, and Vernon 2005; Vernon, Golec, Lutter, et al., 2009; Golec, Hegde, and Vernon, 2010). Reduced cash flows from greater generic utilization reduce, ceteris paribus, the brand firm's level of internal cash flows, which reduces the equilibrium level of R&D investment.

Having illustrated and discussed the ways in which increasing generic utilization rates will reduce the expected IRR of a firm's R&D projects, thereby lowering the expected profit maximizing level of R&D intensity, we now turn to the theoretical model employed by Grabowski and Vernon (1981, 2000); Vernon (2005); Giaccotto, Santerre, and Vernon (2005), and Vernon, Golec, Lutter (2009), upon which our current empirical model is also based.

First, consider the following equilibrium condition for the level of pharmaceutical R&D expenditures:

$$f(X, Y, R) = h(Z, R) \qquad (2)$$

In equation (2): X is a vector of variables influencing the expected costs of an R&D project (e.g., clinical development costs, marketing costs, etc.); Y is a vector of variables influencing the expected revenues from the R&D project (e.g. real U.S. drug prices or generic utilization rates); Z is a vector of variables influencing the firm's cost of capital (e.g., the level of cash flows if market imperfections exist in the capital markets for pharmaceutical R&D; and, R is the level of R&D expenditures. Solving equation (2) for R yields the equilibrium level (expected-profit-maximizing level) of R&D expenditures:

$$R^{*} = g(X, Y, Z) \qquad (3)$$

This is the reduced form equation for equilibrium R&D investment. To obtain our estimate of the elasticity of R&D intensity to generic utilization rates, we will build directly off of the empirical findings from Giaccotto, Santerre, Vernon (2005), who estimated the elasticity of R&D intensity to real U.S. drug prices to be 0.583. This elasticity measure is approximately equal to a similar empirical estimate by Scherer (1996) of 0.61, and is generally plausible.[8] Real U.S. drug prices, which formed the key variable in the Y vector of equations (2) and (3) in Giaccotto, Santerre, Vernon (2005), are influenced by the rate of generic utilization. The reason why increases in generic utilization influence the index of drug prices is primarily a result of how generic drugs are introduced into the index. When a generic enters the index, the U.S. Bureau of Labor Statistics (BLS) will replace the price of a branded drug with the price of its generic equivalent, leading to a large drop in the price of that drug in the index.[9] By marrying the

[8] Here the pharmaceutical CPI was used rather than the PPI. This was because PPI data were not available for the full time series used in the paper by Gianccotto, Santerre and Vernon (2005). To link to the results in that paper, we use the same price measure.

[9] See www.bls.gov/cpi/cpifact4.htm : "Six months after a drug in the sample loses patent protection, CPI field staff selects among all drugs (including the original) that the Food and Drug Administration deems to be therapeutically-

elasticity of R&D intensity to the real U.S. drug price, and the elasticity of the real drug price to generic utilization, we obtain our elasticity of R&D intensity to the generic utilization rate. We express this below using the following implicit formulation of the equilibrium level of R&D equation:

$$R^{*} = g[X, Y(GUR), Z(GUR)] \quad (4)$$

In equation (4), we show that expected future generic utilization rates influence equilibrium R&D investment implicitly through the expected returns and cash flow variables in the Y and Z vectors. As previously discussed, the GUR will directly affect the real U.S. drug price index, and, as a result, expected future profitability and industry cash flows. We now turn to a description of our data and a more explicit specification of our empirical model.

III. Empirical Model Linking Generic Utilization Rates and Real Drug Prices

On the basis of the preceding discussion and our conceptual model depicted in equation 4, we specify, in equation 5, a reduced form model of how the generic utilization rate (GUR) influences real pharmaceutical prices in the U.S. For consistency, we maintain the same measure of real drug prices used in Giaccotto, Santerre, and Vernon (2005), and specify it as a function of the generic utilization rate and other variables that may affect real drug prices. As with Giaccotto, Santerre, and Vernon (2005), there is a high degree of serial correlation in our time series data, and we require second differencing to remove it—in order to avoid the econometric

equivalent. Delaying the reselection for six months allows emerging generic drugs an opportunity to gain market share… If a generic is selected, the CPI treats any price difference between the original drug and its selected substitute as a price change, and reflects this change in the index in the month when the procedure was performed."

difficulties associated with non-stationary processes.[10] We also logarithmically transform our levels variables; hence, our coefficient estimates are interpretable as elasticities, with β_1 in equation (5) serving as an approximation of the elasticity of real U.S. drug price to the generic utilization rate. Because the data we have on generic utilization rates come from IMS, which only has these data going back to 1992, we are not able to re-estimate the model in Giaccotto, Santerre, and Vernon (2005) directly, which relied on annual data from 1953 to 2001. Our model, therefore, uses data between 1992 and 2008. We specify the following model using semiannual data (where Δ represents second differencing):

$$\Delta \ln(P_t) = \beta_0 + \beta_1 \Delta \ln(GUR_{t-1}) + \beta_2 \Delta \ln(UE_t) + \beta_3 \Delta \ln(GDP_t) \qquad (5)$$

In equation (5), P_t is the U.S. prescription drug consumer price index (RxCPI) divided by the, general U.S. consumer price index (CPI), as defined and measured by the BLS. The GUR_t variable is measured by the share of total prescriptions accounted for by generic prescriptions in the IMS Health's National Prescription Audit database. The variables UE_t and GDP_t are controls, and are described shortly.

In measuring the RxCPI, the BLS only registers a change due to generic entry six months after a generic comes on the market. At this point, the BLS may substitute the price of the branded drug with the price of its generic equivalent if the generic version has captured a large share of the brand drug's sales. Thus, based on the way BLS constructs the RxCPI, it is appropriate to lag the generic utilization rate by 6 months (or one period in this model). Given

[10] Dickey-Fuller test statistics is -6.2 on second differenced log of drug prices and -10.2 on second differenced lagged log of generic utilization.

this six month structure in the index for generic entry, the most sensible approach was to use a period of six months (or semi-annually). This left us with 27 observations for the analysis.

The other explanatory variables included are: the unemployment rate (UE_t), as measured by the BLS, and real GDP (GDP_t), all in 2000 dollars.[11] The results of the model described in equation (5) are presented in Table 1 below:

Table 1: Regression Results Explaining Real U.S. Drug Prices

Equation (5) OLS Regression Results: Semiannual Data from 1992-2008

Explanatory Variable	Coefficient Estimate	Standard Error	*t*-Stat	*p* value
Intercept	-0.0015	0.0011	-1.29	0.208
$\Delta \ln GUR$	-0.1506	0.0716	-2.10	0.047
$\Delta \ln UE$	0.0724	0.0224	3.23	0.004
$\Delta \ln GDP$	0.4088	0.1602	2.55	0.018
Number of Observations = 27				
Adj R-squared = 0.3782				
Durbin Watson Statistic = 1.8				

As shown in table 1, and as expected, the generic utilization rate has a negative and statistically significant relationship with real drug prices.[12] The coefficient estimate of -0.15 indicates that with a 10 percent increase (decrease) in the utilization rate, there will be a 1.5 percent decrease (increase) in real drug prices. The two control variables included in the model

[11] We also ran a larger specification of the model that included the following additional variables: (1) the share of the population covered by health insurance (HI) as measured by the census bureau; (2) monthly drug expenditures in dollars (RX), available from the Bureau of Economic Analysis' (BEA) National Economic Accounts database; (3) a measure of drug innovation (IN), defined as the share of new FDA drug application approvals accounted for by new chemical entities (data from the FDA's Center for Drug Evaluation and Research), and (4) the measure of the US population (Pop) taken from the Census.. However, none of these variables was statistically significant and the results were qualitatively the same and quantitatively similar.

[12] Newey-West standard errors generate the same conclusions.

also had statistically significant coefficient estimates. An increase in the unemployment rate is *positively* correlated with real drug prices. Because real drug prices are a ratio of drug prices and the CPI, this result may be picking up a historical relationship between unemployment and the CPI. It may also reflect persistent purchases by unemployed patients that no longer have access to relatively advantageous prices for drugs.[13] Finally, GDP is also positively correlated with real drug prices (indicating that GDP pushes drug prices up more quickly than overall consumer prices).

IV. The Relationship between Increased Generic Utilization and R&D.

There are two primary mechanisms by which increased generic utilization reduces the equilibrium level of R&D investment: a cash-flow effect and an expected-returns effect. As to the first, many firms have portfolios of products on the market at, or near, patent expiration. Generic entry into these markets has an immediate impact on firm cash flows. As to the second, greater generic entry at patent expiration reduces the expected returns to investments in current R&D projects. This effect will be greater the farther along an R&D project is in the development process, as generic erosion will have a greater expected present value impact on expected returns for these projects[14]. Note that products in the same therapeutic class are subject to generic erosion at the expiration of the first-in-class product's patent expiration. Also, to the extent there is off-label use of the relevant products, generic erosion can also affect expected returns to

[13] Note, the model without unemployment also produces a statistically and economically significant coefficient for the generic utilization rate of similar magnitude (-0.12).

[14] This is particularly true given the well-known fact that a project's cost of capital is not constant, but rather higher, on average, the earlier it is in product development; thus resulting in even steeper discounting of future cash flows for earlier-stage R&D projects.

products in different therapeutic classes. The literature has identified these two determinants, current cash flows and expected returns on future products, as the key variables influencing equilibrium R&D intensity. As shown previously in figure 3, increased generic utilization rates will shift the marginal efficiency of R&D (the demand for R&D) to the left, resulting in a lower level of equilibrium R&D expenditures.

A primary research objective in the current paper is to estimate the elasticity of R&D intensity with respect to the generic utilization rate. To this end, we rely on the estimated elasticity of 0.583 for R&D intensity with respect to the real U.S. pharmaceutical price obtained by Giaccotto, Santerre, and Vernon (2005), and our empirical results from table 1. We may express the elasticity measure we seek as a function of these two variables as follows (where $\varepsilon_{i,j}$ is the elasticity of *i* with respect to *j*):

$$\varepsilon_{RD,P} \times \varepsilon_{P,GUR} = \varepsilon_{RD,GUR} \tag{6}$$

Our estimate of the elasticity of real drug prices to generic utilization rates is -0.1506, as shown in table 1. The coefficient estimate is significant at the 0.05-level for a two-tail test and at the 0.01-level for a one-tail test. Using equation (6), it is straight forward to calculate the elasticity of R&D intensity with respect to generic utilization rates in the U.S. This elasticity is estimated to be -0.088 (the product of the previously estimated elasticity of R&D intensity to drug prices, 0.583, and our current estimate of the elasticity of real drug prices to generic utilization, -0.1506). This suggests that for every 10 percent increase (decrease) in generic utilization rates, R&D intensity decreases (increases) 0.88 percent, or, slightly less than 1 percent. This magnitude seems quite plausible in light of the significant amount of discounting

(due to long time horizons) of the revenue shares captured by generics, and associated with greater generic utilization rates, at patent expiration. However, this modestly-sized elasticity, when considered alongside the significant increase in generic utilization rates in the U.S., from 19 percent in 1984 to 69 percent in 2008, suggests the effect on R&D investment is far from trivial. For example, measuring the percentage change in the generic utilization rate as 0.50/0.44, where 0.44 = 0.50(0.19+0.69), implies a 114 percent increase in the generic utilization rate, and hence an associated 10 percent decline in R&D intensity. Based on previous analyses of the social welfare benefits associated with pharmaceutical R&D investment, the present value cost of a 10 percent decline in R&D investment could be very significant (Lichtenberg, 2002; Vernon, 2004). The benefits to consumers of lower U.S. drug prices, via increased generic utilization, would need to be weighed simultaneously with the long-term costs associated with diminished rates of pharmaceutical innovation.

V. Conclusions

Our analyses in this paper provide a measure of the relationship between generic utilization rates and real pharmaceutical prices, in the U.S. Further, relying on prior research, we also measure the relationship between generic utilization rates and R&D investment intensity. We have been able to demonstrate a negative relationship between the level of generic drug utilization in the U.S. and real U.S. pharmaceutical prices. Our results, when coupled with prior research, are consistent with the expectation, implied by theory, of higher levels of generic utilization in the U.S. resulting in lower levels of profit-maximizing, equilibrium R&D investment intensity. The primary drivers underlying this relationship are the aforementioned

effects generic utilization rates have on cash flows (the primary source of funds for R&D due to their lower cost of capital relative to debt and equity) and expected returns to pharmaceutical R&D investment.

Since the Hatch-Waxman Act of 1984 attempted to balance drug innovation and generic competition, utilization rates have risen from 19 percent to approximately 70 percent. An important question is whether or not the Hatch-Waxman Act initially (and subsequently—i.e., today), achieved (achieves) the right balance. Previous research by the CBO suggests that there has been an imbalance, see, e.g., Cook (1998). Moreover, research by Murphy and Topel (2003) and Lichtenberg (2002), suggests that, based on contributions to life expectancy and quality of life, medical and pharmaceutical R&D are likely to be at inefficiently low levels.

Of course, markets change over time and some of the imbalance may be an unintended consequence. While research and development costs have increased, so too has spending on pharmaceuticals. Greater levels of generic drug utilization, new laws and policies, changing FDA approval requirements, and the evolution of science have all contributed to a very different pharmaceutical market.

The results in this paper provide an important input to any balancing of the benefits of access to existing medicines and the costs of foregone innovation. While it is difficult to assess this balance, it seems likely that over the last three decades, the growth of generic utilization has shifted toward access, at some cost in innovation. Specifically, generic utilization rates since Hatch-Waxman have grown 50 percentage points: from 19 percent to 69 percent. This is approximately a 114 percent increase. Based on the results in this paper, this would imply,

ceteris paribus, that R&D intensity has declined by about 10 percent.[15] These results not only help to diagnose an imbalance, but also provide a start on moving forward towards a remedy. Future research that can reasonably measure both the costs and benefits of changing market structures, institutional changes (e.g. FDA policies and approval requirements), and proposed new regulations, will be of much value to the extent it can inform and shape public policy, in an effort to minimize the sum of static (short-run) inefficiency costs and dynamic (long-run) inefficiency costs—thus striking an economically efficient balance between access to existing pharmaceuticals and appropriate incentives for the discovery and development of future medicines.

[15] 1.14*0.088 is approximately 0.10. Note, this should not be interpreted as a measurement of the impact of the Hatch-Waxman Act on R&D, which would require an assumption that—but for the Act—the generic utilization rate would still be 19 percent, and we do not have a measure of how different the generic utilization rate would have been in the absence of the Act. Moreover, such questions are beyond the scope of this paper.

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