NBER WORKING PAPER SERIES

HAS THE EUROPEAN UNION ACHIEVED A SINGLE PHARMACEUTICAL MARKET?

Aysegul Timur
Gabriel Picone
Jeffrey S. DeSimone

Working Paper 16261
http://www.nber.org/papers/w16261

NATIONAL BUREAU OF ECONOMIC RESEARCH
1050 Massachusetts Avenue
Cambridge, MA 02138
August 2010

We appreciate helpful comments from participants in a seminar at the University of South Florida and a session at the 2008 SEA meetings. The views expressed herein are those of the author and do not necessarily reflect the views of the National Bureau of Economic Research.

Has the European Union Achieved a Single Pharmaceutical Market?
Aysegul Timur, Gabriel Picone, and Jeffrey S. DeSimone
NBER Working Paper No. 16261
August 2010
JEL No. I11

ABSTRACT

This paper explores price differences in the European Union (EU) pharmaceutical market, the EU's fifth largest industry. With the aim of enhancing quality of life along with industry competitiveness and R&D capability, many EU directives have been adopted to achieve a single EU-wide pharmaceutical market. Using annual 1994–2003 data on prices of molecules that treat cardiovascular disease, we examine whether drug price dispersion has indeed decreased across five EU countries. Hedonic regressions show that over time, cross-country price differences between Germany and three of the four other EU sample countries, France, Italy and Spain, have declined, with relative prices in all three as well as the fourth country, UK, rising during the period. We interpret this as evidence that the EU has come closer to achieving a single pharmaceutical market in response to increasing European Commission coordination efforts.

Aysegul Timur
Johnson School of Business, Hodges University
2655 Northbrooke Drive
Naples, FL 34119
atimur@hodges.edu

Gabriel Picone
Dept. of Economics
University of South Florida
4202 E. Fowler Ave.
Tampa, FL 33620
gpicone@coba.usf.edu

Jeffrey S. DeSimone
Department of Economics
University of Texas at Arlington
701 S. West St.
Arlington, TX 76019
and NBER
jdesimone@uta.edu

1. Introduction: The EU Pharmaceutical Market

Since 1985, one goal of the European Commission has been to achieve a single market for the pharmaceutical industry. The purpose of harmonizing the European Union (EU) pharmaceutical market is not only to provide an environment favorable for pharmaceutical innovation and development, but also to improve consumer choices in pharmaceuticals at affordable prices without compromising quality, safety or efficacy (European Commission 1998). However, efforts have been hampered by differences across countries in health system characteristics such as government market power and regulation, reimbursement policies and patent processes. Without a centralized approach to pharmaceuticals, EU members continue to apply their own individual solutions. Such segmentation could increase costs for the industry and for patients if there are efficiency gains to having a more coordinated market.

Variation in health system regimes across EU member states creates cross-country differences in prices for the same pharmaceutical product (Drummond 2003). National governments often determine prices independently of market mechanisms. Appendix table A-1 lists differences in characteristics of the five major EU pharmaceutical markets. While attempting to slow rapidly rising health care costs, national governments have implemented policies ranging from direct price controls and supply side cost containment regulations to demand side financial incentives, quantity controls and physician educational initiatives (Kanavos 2001;Mossialos, et al. 2004). Strategies employed by the European Commission to narrow the divergence among the different national markets have included the organization of several round table discussions and the creation of the European Agency for the Evaluation of Medicinal Products (EMEA), European Patent Systems, the G10 Medicines Group and, most recently, the Pharmaceutical Forum.

A particularly important issue has been parallel importing. This occurs when a drug is purchased in another country and then sold in the home country, at a price higher than the purchase price but lower than the prevailing home country price (Darba and Rovira 1998). EU parallel imports of pharmaceuticals were estimated at €4.265 billion in 2003, representing a dramatic increase from a decade earlier and 5% of overall market value (EFPIA 2005). In 2005, one of every 17 prescriptions in the United Kingdom was filled with a parallel import, accounting for about one-seventh of total sales (The Association of the British Pharmaceutical Industry 2007). This implies that arbitrage opportunities have persisted despite efforts to coordinate the market, perhaps aided by lower repackaging costs in conjunction with EMEA harmonization of dosage and labeling requirements. At the same time, parallel imports should encourage pharmaceutical price convergence by dragging down prices in countries where pharmaceuticals are more expensive (OECD 2000;Towse 1998). For instance, Ganslandt and Maskus (2004) found that the prices of drugs subject to competition from parallel imports fell relative to those of other drugs by 12–19%.

The purpose of this paper is to investigate recent trends in EU pharmaceutical price differences. Our analysis employs molecule-level IMS Health data on drugs that treat selected cardiovascular diseases, covering the five countries with the largest pharmaceutical markets in the EU over the 1994–2003 period. We proceed in three steps. First, we estimate trends in bilateral price differences using quasi-hedonic regressions that control for variation in drug characteristics. Second, we examine the contribution of various product and market characteristics to price dispersion using a quasi-hedonic regression that permits intercepts and parameters to differ across both countries and time. Third, we decompose price differences into portions attributable to quality and market competition, along with an unexplained residual,

using parameter estimates from the fully-interacted hedonic model.

2. Data

2.1. Characteristics

International pharmaceutical price comparisons, which have been the subject of several empirical studies, are confronted with various practical difficulties regarding the utilization of price data. One problem is that the packaging unit in the country that serves as the basis for comparison might be uncommon or even unavailable in other countries (Berndt 2000;Berndt, et al. 2002). Another problem, which is mitigated in recent data on EU countries that use the euro (€) as the local currency, is how to standardize different units of exchange. Conversions are typically made using Purchasing Power Parities (PPP), but the applicability of the general PPP to the health care sector is variable and uncertain. A third problem is the decision regarding which set of medications to examine (Barry, et al. 2004). Yet another question is whether to further normalize the price according to the WHO-defined daily dose (DDD), which assumes that standard treatment duration is uniform across countries (Danzon and Chao 2000).

Danzon (1999) recognized that samples consisting solely of packs sold in different countries with the same ingredient, manufacturer, brand name, dosage form, size and strength would exclude generic and over-the-counter (OTC) products. Because generics and OTCs likely serve as substitutes for originator and prescription drugs, respectively, their omission could yield unrepresentative samples (Hellerstein 1998), a problem potentially exacerbated by not including all forms and strengths (Ellison, et al. 1997;Scherer 1993;Scherer 2000). The solution developed by Danzon (1999) is to identify a drug by its active ingredient, i.e. molecule, and anatomic therapeutic category (ATC) without regard to manufacturer or brand name.

Likewise, we combine all forms of a given molecule, including generics and licensed products, to form a weighted average price per molecule-ATC. Ignoring differences between identical molecules within the same ATC is seemingly less problematic than prospectively introducing selection bias by systematically excluding various substitutes, forms, pack sizes and strengths. We use the three-digit, i.e. third level, ATC, although results change little if we disregard ATC and identify each drug simply by its molecule.

This paper employs data from IMS Health, an international pharmaceutical consulting company that collects sales data on more than one million products from over 3,000 companies in more than 100 countries. The IMS Health measure that meets the criterion of being available for all dosage forms and strengths is the IMS Standard Unit (SU). The SU defines a single dose as one tablet or capsule, five liquid milliliters (i.e. one teaspoon), or one ampoule or vial of an injected product (IMS 2005). Prices are converted to euros by IMS Health using constant exchange rates, which minimizes effects of exchange rate fluctuations. A country's SU price for a molecule-ATC is its volume-weighted average price per dose over all presentations, including generic, licensed, OTC, and parallel imported products (Danzon and Furukawa 2003).

2.2. Samples

We analyze retail prices of drugs that treat cardiovascular disease (CVD), the third-leading cause of death in OECD countries. Importantly, the effectiveness of CVD drug therapies is short-term, so patients must continually receive a treatment to maintain its health benefits. Our sample consists of the eight CVD drugs studied by Dickson and Jacobzone (2003), which cover both newer and older innovations that form the core of pharmacotherapy for CVD.

The five countries in the sample are Germany, the United Kingdom (UK), Italy, Spain,

and France. Besides having the largest pharmaceutical production and sales in the EU-15 (OECD 2003), these five countries are the largest pharmaceutical markets in the world apart from the US and Japan (Pammolli, et al. 2004). Imposing the previously described restrictions, our sample would contain 259 distinct single molecules, representing 658 molecule-by-country cells during the 1994–2003 period: 119 for France, 177 for Germany, 135 for Italy, 119 for Spain and 108 for UK. An additional constraint, which unfortunately is substantial, accompanies the necessity of choosing a baseline country with which to compare the others. We choose Germany for this role because, as listed above, it contains the most molecules by a wide margin. Our sample is thus limited to the 124 single molecules – 86 each for France and UK, 102 for Italy and 91 for Spain – that bilaterally match with Germany.

2.3. Preliminary Price Comparisons

As shown in Table 1, the average SU price over all molecules and years ranges from €0.24 in Spain and €0.25 in Italy and France to €0.60 in Germany and €1.36 in UK. Table 2 and the accompanying figure depict average yearly SU prices for each country relative to that of Germany, reiterating that prices are substantially higher in UK than Germany while prices in the other three countries are substantially lower. After decreasing slightly in the latter 1990s, the France-Germany price differential increases from –55% in 2000 to –72% in 2003. Similarly, the Italy-Germany price gap rises from –63% to –71% over the period, while the Spain-Germany price difference rises from –68% to –78%. In comparison, the UK-Germany price wedge expands considerably during the period, to almost 200% by 2003.

These trends seemingly indicate that pharmaceutical prices across countries are diverging, rather than converging as if spurred by the achievement of a single market. However,

the table 2 prices have not yet been adjusted for variation in the set of molecules sold in each country. Some of these price differentials might be attributable to systematic differences in the characteristics of drugs available in some countries but not others.

3. Differences in Prices Adjusted by Quality and Market Competition

3.1. Quasi-Hedonic Price Regressions

When making international price comparisons, cross-country differences in product specifications pose an obstacle (Kravis and Lipsey 1969). Products serving the same purpose might have different attributes in different countries. For example, a Honda Accord might have varying horsepower across countries, or come with automatic transmission in some countries and manual transmission in others (Goldberg and Verboven 2004). In our case, the forms, pack sizes and strength levels in which drugs are sold vary across countries, depending on demand and cultural characteristics. To address this issue, we use hedonic regressions.

As Danzon and Chao (2000) note, our price models are more appropriately termed quasi-hedonic regressions for three reasons. First, while the standard hedonic model assumes that price determinants differ randomly across products, pharmaceutical prices are expected to differ systematically across countries, reflecting differences in health care regimes. Because some price variation across countries is explained by factors other than observed product characteristics and that change very little over time, the models include country-specific intercepts. Second, hedonic regression estimates the marginal contribution of each characteristic to the value of a product (Sirmans et al. 2005). However, pharmaceutical market imperfections drive a wedge between price and marginal value. These include deviations between patient and physician preferences, moral hazard from insurance coverage, and monopsony power of national

health systems on the demand side, along with patent restrictions providing monopoly power to producers and marketing restrictions through drug approval and testing requirements on the supply side (Capri and Levaggi 2005). Third, drug prices also vary across countries because of time-varying differences in regulatory and reimbursement environments. To address this, our models specify market competition measures, which would not appear in a standard hedonic regression, as additional explanatory variables.

3. 2. Specification of the Quasi-Hedonic Price Regression

Adapted from Danzon and Chao (2000), our model uses log transformations of product prices and characteristics,

$$(1) \quad \ln P_{k,j,t} = \alpha + \beta_c \sum_{c=1}^{8} \ln X_{c,k,j,t} + \sum_{t=1}^{9} \varphi_t d_t + \sum_{j=1}^{4} \phi_j d_j + \sum_{t=1}^{9}\sum_{j=1}^{4} \lambda_{j,t} d_j d_t + \sum_{k=1}^{K} \delta_k d_k + u_{k,j,t}.$$

In equation 1, for molecule k in country j and year t, P is the price per SU and X_c is a quality or market characteristic. The d are indicators for country, year or molecule, while u is the regression error. The parameter of primary interest, $\lambda_{j,t}$, estimates the average bilateral price difference in time t between country j and Germany, which is omitted from the country indicator vector, across molecules. This price gap is net of variation induced by differences across quality and market characteristics, molecules, time or countries.

Our preferred specification treats the molecule-specific intercepts as fixed effects by including molecule indicators on the right-hand side. Besides the molecule quality and market characteristics that appear in equation (1), drug prices also reflect therapeutic value and convenience, attributes that have intrinsic value but are not observable. If these are time-invariant and molecule-specific, the fixed effects model is appropriate. An alternative approach is to hold constant ATC indicators as proxies for market and regulatory factors that vary by ATC

category. Because these are time-invariant, however, they are not identified in the fixed effects model. We therefore also estimate a random effects model. This strategy accounts for the molecule-specific intercepts in the error term, and thus the regression standard errors, but does so by invoking the questionable assumption that these intercepts are uncorrelated with the molecule characteristics as well as the indicators for molecule, country and year.

3.2.1. Description of Variables

Table 1 lists the variables along with their descriptive statistics. We categorize the first five variables in the table as quality characteristics. Molecule age is the number of years since the first product launch of molecule *k* in country *j*. The sample mean is 20 years, ranging from 18 in Spain to 22 in UK. We expect molecule age to be inversely related with price, since newer treatments are typically introduced precisely because they are more effective, and thus have higher value, than older treatments. Most molecules in our CVD ATCs were on the market prior to the sample period.

Strength is the average grams of active ingredient per SU and ranges from 0.14 in France and UK to 0.23 in Spain, with an overall mean of 0.17. Stronger molecules are presumably more effective, holding constant technological developments for which molecule age proxy, implying a positive association between strength and price.

Form code is the number of different product formulations for each molecule, and is intended to reflect choice and convenience available to patients, suggesting a positive relationship with price. Forms include different types of tablets (e.g. film, chewable, gel), capsules, ampoules, powders, drops, syrups, syringes, and liquids, along with different strengths and pack sizes. In 2003, for example, the molecule metoprolol (in ATC C7A) was available in

118 different formulations in Germany. The mean is 6, ranging from 3 in France, Italy and Spain to 12 in Germany.

Pack size is the number of SUs averaged over all packs in a molecule, converted to standard units according to IMS (2006) guidelines. If manufacturers achieve economies of scale in packaging, price and pack size will be inversely related. The average SU pack size ranges from 28 in Italy to 85 in Germany, with an overall mean of 56.

The final quality characteristic, diffused molecules, is simply the number of sample countries in which the molecule is available, and thus varies only between 2 and 5. If drug manufacturers market a product wherever its marginal revenue exceeds its marginal cost, diffusion will increase as marginal revenue rises or marginal cost declines. Net of institutional differences captured by country fixed effects, therefore, diffusion could reflect either higher therapeutic values or lower costs, making the theoretical relationship with price unclear. However, if the other characteristics held constant in the model are correlated mostly with therapeutic value rather than cost, a negative coefficient on diffusion will emerge.

The last two rows list the time-varying market characteristics included in the fixed effects model. Both reflect increased availability of substitutes and should thereby be negatively related with price. Generic competitors are manufacturers of products containing the molecule, including originators, licensees, parallel imports and generics. The average is eight in Germany, but only three in the other four countries. Therapeutic substitute molecules are competitors that are chemically distinct but used to treat the same indication, i.e. the number of molecules within the same ATC3. On average, Germany again has the most, 22, while UK has the least, 13.

3. 3. Empirical Results of the Quasi-Hedonic Price Model

3.3.1. Quality and Market Characteristics

Table 3 contains the results of fixed and random effects estimation of equation (1). Because all variables are specified in log form, each coefficient is interpreted as the elasticity of price with respect to the corresponding quality or market characteristic. Most regressors have the expected sign and are statistically significant. Except for molecule age, which in the fixed effects model is identified only through the nonlinearity introduced by the log transformation, the fixed and random effects models yield similar conclusions.

The average SU price rises with product strength. This is not surprising, because reference pricing based on product attributes, which is widely employed in the sample countries, incorporates a positive relationship between strength and therapeutic effectiveness that presumably must exist to justify selling different drug strengths. The coefficients imply that a 10% increase in molecule strength raises price by 2–3%, with the more conservative estimate coming from the random effects model.

The molecule age coefficient in the fixed effect model, which is near zero and highly insignificant, conveys little information because within-molecule age varies separately from the fixed year and molecule effects only via the non-linearity of the log transformation. An advantage of the random effects model, therefore, is its utilization of cross-molecule variation to estimate the relationship between price and molecule age. The significantly negative coefficient is consistent with the notion that relative therapeutic value declines with age as more effective new products enter the market. A 10% increase in age reduces price by about 2%.

The number of formulations is insignificantly related to price in both models. Price decreases significantly with pack size, though, as implied by economies of scale in packaging, EMEA packaging and labeling regulations, and use in reference pricing calculations. Both

models imply that the price of a 10% larger pack size will be lower by about 4%.

Consistent with earlier studies, price also declines significantly with the number of diffused molecules. The implied elasticity is nearly –0.4 with fixed effects, but only around –0.2 with random effects.

Among the market characteristics, only generic competition is significantly related with price, and only in the random effects model. Generic competition reduces price, as expected, but by well less than 1% for each 10% increase. The impact of generic competition might have been mitigated by the addition of generic substitution to the regulatory systems of many EU countries by the late 1990s. In 1993, the EU introduced legislation allowing supplementary patent certificates (SPCs) that, analogous to the Roche-Bolar provision of the Waxman-Hatch Act in the US, allows generic manufacturers to develop versions of products that are still under patent protection. SPC applications must go through a specific national patent office, giving member countries the opportunity to separately address the issue. In Germany and UK, generic suppliers can formulate and test products and complete product review in another country while the patent is active, which can substantially reduce the time between patent expiration and generic launch. For example, German generics have been launched the day following patent expiration. In France, meanwhile, required documentation cannot be submitted for review until after patent expiration, delaying the launch of generic competition for up to five years.

The number of therapeutic substitute molecules is not significantly related to price, as opposed to the inverse relationship that is expected and that Danzon and Chao (2000) obtain in their data. Our result is not attributable to the inclusion of fixed effects, since the coefficient is very similar in the random effects model. Substitute molecules with a higher price might not receive reimbursement, and substitution is not always possible in regulated countries because of

prescribing or consumption preferences.

The therapeutic substitute entry lag, in years, is a time-invariant market characteristic identified only in the random effects model. Its coefficient is positive but insignificant.

3.3.2. Quality Adjusted Standard Unit Price Differentials

An important purpose of the equation (1) regression is estimating the country-by-year interaction coefficients. These represent country-specific price trends that are unrelated to quality and market characteristics, molecule identity, time-invariant country-specific factors and temporal factors common to the sample countries. Table 4 shows the percentage differences in price, relative to Germany, implied by these interaction coefficients.

Over time, price differences persist, but decline in magnitude. This likely reflects increasing market integration for several reasons, including parallel importing and greater monitoring of cross-country price differences by the EU Commission in an effort to achieve a single pharmaceutical market.

Prices in France, Italy, and Spain move similarly, consistent with growing comparability of their pharmaceutical industries and regulatory environments. For each drug, the French government negotiates a single price targeted to the EU average. Changes implemented in the late 1990s and early 2000s include increased promotion of generic substitution by pharmacists, financial incentives for patients to visit general practitioners rather than more expensive specialists, and price cuts on expensive drugs such as Zocor. Spain likewise has fixed drug prices and uses international comparisons for reference pricing of generics, with prices set 10–50% below those of the original brand in order to induce branded drug price reductions. Drugs on a negative list are not reimbursed, and in 2001 price cuts of 15% were imposed for a variety

of molecules. Italy's regulatory approach is similar, with fixed pricing and cost-effectiveness analysis of in-patent drugs. Prices of both branded and generic drugs are based on those in other EU countries, and drugs with identical or therapeutically comparable pharmaceutical forms must have the same price per unit. In 1999, price cuts of 15% were implemented for many products, and the following year prices on unprotected branded drugs were reduced another 5%.

Once quality and market characteristics are held constant, prices are higher in Germany than in the other countries, including UK. Health care systems in Germany and UK, though distinct, are alike in several respects. Although Germany is the only sample country with unrestricted in-patent drug prices, a reference pricing system governs older products, and pharmaceutical budgets and spending caps have been implemented since the 1980s. Health insurance reimburses all pharmaceutical products not on the negative list, and both parallel imports and generics are well-established. UK regulates in-patent drugs using cost-effectiveness analysis and profit control. Government negotiates prices of licensed and branded drugs with the pharmaceutical industry, and prices of generics are now also regulated because of recent increases. Parallel imports from elsewhere in Europe are also encouraged.

4. Further Analysis of Price Differentials: Explained vs. Unexplained

This section expands on the equation (1) model to estimate how the price effects of molecule characteristics vary across countries and over time. For each country, these parameters are used to partition the trends in bilateral price differences with Germany into a portion attributable to differences in mean values of the quality and market characteristics, with the remainder attributable to differences in parameter values or fixed country effects.

4.1 Fully-Interacted Model

4.1.1. Specification

The new model generalizes equation (1) by allowing molecule characteristics to have different effects in different countries and years. This is done by adding interactions between characteristics and country fixed effects, year fixed effects and country-by-year fixed effects. The updated model is thus

$$(2)\quad \ln P_{k,j,t} = \alpha_0 + \sum_{c=1}^{7}\beta_c \ln X_{c,k,j,t} + \sum_{j=1}^{4}\phi_j d_j + \sum_{t=1}^{9}\varphi_t d_t + \sum_{t=1}^{9}\sum_{j=1}^{4}\lambda_{j,t} d_j d_t + \sum_{c=1}^{7}\sum_{j=1}^{4}\rho_{c,j} d_j \ln X_{c,k,j,t} + \sum_{c=1}^{7}\sum_{t=1}^{9}\gamma_{c,t} d_t \ln X_{c,k,j,t} + \sum_{c=1}^{7}\sum_{t=1}^{9}\sum_{j=1}^{4}\theta_{c,j,t} d_j d_t \ln X_{k,j,t} + \sum_{k=1}^{K}\delta_k d_k + u_{k,j,t}.$$

Variables and parameters are denoted as in equation (1), and ρ, γ, and θ are the coefficients on the new interactions between the molecule characteristics and the country/year indicators. Net implicit prices for molecule characteristics are β for Germany in 1994, ($\beta + \gamma_t$) for Germany in year t = 1995–2003, ($\beta + \rho_j$) for other countries j in 1994, and ($\beta + \gamma_t + \rho_j + \theta_{j,t}$) for other countries j in year t = 1995–2003.

4.1.2 Empirical Results

The estimated elasticities of price with respect to quality and market characteristics are summarized in table 5 for 1994 and 2003. Coefficient directions are largely consistent with our earlier results, although magnitudes sometimes differ substantially across countries.

Price is increasing in strength per SU, as expected, in all countries and years. Strength elasticities are largest in Germany, possibly because strength is directly used to determine relative prices, and larger in UK than remaining countries. Molecule age is significantly negatively related to price in France, Italy and Spain, in each of which fixed prices prospectively

encourage renegotiation of lower prices as molecules age (Mossialos et al. 2004, Seget 2003), with the magnitude rising over time in Spain but falling over time in France and Italy. The number of formulations significantly increases price in France during the first half of the period and in Italy and Spain throughout. Again, with fixed prices, introduction of a new formation might provide an opportunity for manufacturers to renegotiate prices upward. The number of diffused molecules significantly reduces price in Italy, perhaps reflecting the use of average EU price comparisons, and UK, which evaluates treatments in terms of both clinical and cost effectiveness. Price significantly decreases with pack size in all countries and years, which is not surprising since, for instance, patient co-payment is based on pack size in Germany and maximum price is based on maximum pack size in UK.

Among the market variables, therapeutic substitute molecule availability affects price negatively in Italy and Spain, in which prices are negotiated between suppliers, physicians and pharmacists. Competition, under therapeutic reference pricing, decreases drug prices (Brekke, et al. 2007). Like pack size, the number of generic competitors significantly reduces prices in all countries and years. The impact is smallest in France and Spain, possibly reflecting regulations on generics and limitations on price negotiations, and largest in UK and Germany, which had unrestricted pricing and significant price reductions in the late 1990s.

4.2. Decomposition of characteristics

This part of the analysis uses the Oaxaca (1973) decomposition method to explain the price differences using the vector of determinants in equation (2). Specifically, we seek to establish how much of the price difference between each country and Germany in a given year is specific to observed quality and market characteristics. We decompose each price differential

into three parts: one attributable to differences in the magnitudes of quality characteristics, a second attributable to differences in the magnitudes of market characteristics, and a third residual component which represents the difference between the overall price differential and the first two parts, including differences in the quality and market characteristic parameter values across countries and years as well as differences in the country fixed effects.

4.2.1 Specification

The ratio of mean price of a molecule in country *j* relative to that in Germany, i.e. the approximate percentage price differential, can be written as

$$\ln(P_j / P_{GR}) = \ln P_j - \ln P_{GR} = \beta_j \ln X_j - \beta_{GR} \ln X_{GR}$$

Inserting the term ($\beta_{GR} \ln X_j - \beta_{GR} \ln X_j$) into the right-hand side and distributing accordingly yields the expression

(3) $$\ln(P_j / P_{GR}) = \beta_{GR}(\ln X_j - \ln X_{GR}) + (\beta_J - \beta_{GR}) \ln X_j ,$$

adopted from Danzon and Chao (2000). The first term $\beta_{GR}(\ln X_j - \ln X_{GR})$, called the explained component, represents the difference in mean characteristics of the sample of molecules in country *j* compared with Germany, evaluated using the regression parameters for Germany. In other words, this component is the portion of the price gap attributable to differences in average characteristics between the comparison country and Germany. The second term $(\beta_j - \beta_{GR}) \ln X_j$, called the unexplained component, represents the difference in regression parameters compared to Germany, evaluated using the characteristics in country *j*. This unexplained component measures country-specific price differences arising from differences across markets in how molecule characteristics are "treated." If the coefficients of these characteristics are the same for comparison country *j* and Germany, the unexplained component

equals zero, implying that price differences related to molecule characteristics are attributable entirely to differences in the characteristics themselves. Country intercepts then estimate the residual effects not explained by values or effects of the molecule characteristics.

4.2.2 Empirical Results: Quality vs. Competition Characteristics

Table 6 summarizes the results of the decompositions, using the parameter estimates from the fully-interacted model (2) in section 4.1. For each country relative to Germany, the overall log price difference in each year is disaggregated into the components explained by quality and market characteristics and a total of the three unexplained components, i.e. related to differences in quality and market regression parameters as well as country-specific intercepts.

During 1994–2003, prices in each of the other four countries have risen relative to Germany. For countries other than UK, prices are still lower than in Germany, meaning that the relative price increase represents a convergence in prices. The price difference with Germany has decreased by about 40% for France, 50% for Spain and 65% for Italy. Meanwhile, the UK price has risen from 16% less than Germany to 33% greater. The timing of relative price movements also differed somewhat across countries. In Italy, price convergence was steady starting in 1995. In France, convergence was concentrated during 1994–1997, as the price gap with Germany actually increased over the next five years before falling again in 2003. Spain is similar, with convergence occurring primarily during 1994–1997 and 2001–2003. In UK, prices increased substantially in 1997, 1999 and 2003, making up for a temporary decline in 2002.

Much of this price convergence is predicted by a relative decrease in German drug "quality," i.e. changes in values of quality characteristics that led to prices in Germany falling compared with other countries. For example, of the 18 percentage point convergence in price

between France and Germany, 16 percentage points are attributable to improved quality relative to Germany. Analogous totals for the other countries are 34 of 44 percentage points in Italy, 19 of 33 points in Spain and 22 of 49 points in UK. Thus, it appears that pharmaceutical companies have been largely responsible for EU drug price convergence through lowering the quality of their products in Germany relative to other countries. This is ironic, as prices in the other countries at the start of the period were lower than in Germany in spite of Germany having the lowest predicted price based on quality characteristics.

For all countries, competition has been increasing relative to Germany, in the sense that market factors predict comparatively falling rather than rising prices in the other countries. However, these effects are small, i.e. 10 percentage points in France and Spain and only 5–6 points in UK and Italy.

Unexplained factors, therefore, account for (more than) the rest of the convergence in prices, varying in importance from 13 percentage points in France and 17 points in Italy to 23 points in Spain and 33 points in UK. The unexplained component, which is assumed to capture the net effect of country specific industry dynamics such as insurance coverage, medical norms and reimbursement incentives, was already the reason prices were higher in Germany than elsewhere.

From the detailed decomposition estimates, not presented here but available from the authors, we can further disaggregate the sources of the price changes predicted by each set of factors. Note that based on equation 3 above, "explained" price changes include not only changes in mean characteristic values but also changes in the Germany regression parameters, because we separately estimate equation 3 each sample year. Other than a 15% increase in molecule age, characteristic means changed very little over the period.

The "explained" changes are thus attributable primarily to changes in the Germany regression coefficients. These are driven almost entirely by increases, in absolute value, of the negative coefficient of a specific quality factor, pack size. Multiplied by the essentially unchanged cross-country differences in mean pack size, this predicts relative price increases of 18 percentage points in France, 25 points in Italy, 19 points in Spain and 43 points in UK. These predict changes represent nearly three-quarters of predicted price convergence from quality changes in Italy, 100% in Spain and effectively all of the predicted overall price convergence in France and UK. In particular, 30–60% of these impacts, depending on the country, reflect the change in the Germany pack size regression coefficient just from 1999 to 2000. This suggests a change in the reference pricing formula in Germany, starting in 2000, in which price discounts for larger pack sizes were increased.

Accounting for changes in relative prices attributable to specific "unexplained" factors is more difficult. Increasingly positive pack size coefficients in every country besides Germany are partly responsible, but this is much more important in France than the other countries. Also, changes in each other factor, with the exception of form code, play a central role in at least one country. In France and Italy, relative price increases predicted from changes in unexplained quality factors are mostly offset by large decreases predicted from changes in the residual term, with relatively little change from unexplained competition factors. But in Spain and UK, residual changes predict further relative price increases, whereas unexplained competition factors predict declining prices.

By the end of the period, prices continued to be lower in France, Italy and Spain than in Germany because the negative effect of unexplained factors swamped the positive impact of higher quality. However, price gaps had shrunk both because observed quality differentials had

increased and unexplained differentials had fallen. Meanwhile, prices were higher in UK by 2003 partly because unexplained factors now predicted higher, rather than lower, prices. Higher quality relative to Germany was an even more important factor, although quality was lower in UK than in the other three countries.

5. Conclusion

The purpose of this paper is to analyze price differences across molecules that treat cardiovascular disease across selected European Union countries during 1994–2003. Although pharmaceutical prices are regulated in all five countries that we study, specific regulations vary. For instance, in Italy, France and Spain, prices are regulated at launch and subsequently are revised downwards over the life cycle of the drug. In contrast, pharmaceutical companies in the UK and Germany are free to set prices at launch, although prices cannot move freely throughout the life of the drug.

Our data include only cardiovascular disease drugs in certain therapeutic categories that were sold in the five countries we study and are matched to one country in particular, Germany. Similarly, our data set extends for only a ten year period. Caution must be exercised, therefore, in generalizing our findings to molecules designed to treat other diseases in other countries and more recent years.

Notwithstanding these limitations, three main conclusions can be drawn from our study. First, drug prices in Germany fall relative to prices in other countries over 1994–2003. For countries besides UK, these relative price changes are interpreted as evidence of price convergence. Second, several observed drug characteristics affect prices in the expected way. Third, drug quality in Germany has fallen relative to the other countries, contributing to price

convergence. These results suggest that although price differences still exist because of diverging health system regulations, market integration and continued coordination efforts of the European Commission are moving the EU towards a single pharmaceutical market.

References

Barry, M., Bruzzone, M., DeJoncheere, K., Folino-Gallo, P., Rosian, I., Schroder, H., Tilson, L., and Vogler, S. 2004. "Price Indicators-The Library of European Union Pharmaceutical Indicators." EURO-MED-STAT Group.

Berndt, E.R. 2000. "Editorial: International Comparison of Pharmaceutical Prices? What Do We Know, and What Does It Mean?" *Journal of Health Economics*, 19, pp. 283-87.

Berndt, E.R., Bir, A., Busch, S.H., Frank, R.G., and Normand, S.L.T. 2002. "The Medical Treatment of Depression, 1991-1996: Productive Inefficiency, Expected Outcome Variations, and Price Indexes." *Journal of Health Economics*, 21, pp. 373-96.

Brekke, K.R., Konigbauer, I., and Straume, O.R. 2007. "Reference Pricing of Pharmaceuticals." *Journal of Health Economics*, 26, pp. 613-42.

Capri, S. and Levaggi, R. 2005. Social Science Research Network: Working Paper Series. *International Price Regulations in the Pharmaceutical Sector: A Common Model to Sharing Cost and Benefits*. http://papers.ssrn.com.

Danzon, P.M. 1999. *Price Comparisons for Pharmaceuticals: A Review of U.S. and Cross-National Studies*. Washington, D.C.: The AEI Press.

Danzon, P.M. and Chao, L.W. 2000. "Cross-National Price Differences for Pharmaceuticals: How Large, and Why?" *Journal of Health Economics*, 19, pp. 159-95.

Danzon, P.M. and Furukawa, M.F. 2003. "Prices and Availability of Pharmaceuticals: Evidence From Nine Countries." *Health Affairs*, Web Exclusive.

Darba, J. and Rovira, J. 1998. "Parallel Imports of Pharmaceuticals in the European Union." *Pharmacoeconomics*, 14:1, pp. 129-36.

Dickson, M. and Jacobzone, S. 2003. "Pharmaceutical Use and Expenditure for Cardiovascular Disease and Stroke: A Study of 12 OECD Countries." *OECD Health Working Papers*, DELSA/ELSA/WD/HEA (2003)1.

Drummond, M.F. 2003. "Will There Ever Be A European Drug Pricing and Reimbursement Agency?" *The European Journal of Health Economics*:4, pp. 67-69.

EFPIA. 2005. "The Pharmaceutical Industry in Figures." *European Federation of Pharmaceutical Industries and Associations*, Key Data:2005 update, pp. 1-27.

Ellison, S.F., Cockburn, I., Griliches, Z., and Hausman, J. 1997. "Characteristics of Demand for Pharmaceutical Products: An Examination of Four Cephalosporins." *The RAND Journal of Economics*, 28:3, pp. 426-46.

European Commission. 1998. *The Single Market in Pharmaceuticals*. http://europa.eu.int/scadplus/leg/en/lvb/l21227.htm. February 2009.

Ganslandt, M. and Maskus, K. 2004. "Parallel Imports and the Pricing of Pharmaceutical Products: Evidence From the European Union." *Journal of Health Economics*, 23, pp. 1035-57.

Goldberg, P.K. and Verboven, F. 2004. "Cross-Country Price Dispersion in the Euro Era: A Case Study of the European Car Market." *Economic Policy*, pp. 483-521.

Hellerstein, J. 1998. "The Importance of the Physician in the Generic versus Trade-Name Prescription Decision." *The RAND Journal of Economics*, 29:1, pp. 108-36.

IMS. 2005. *IMS Midas Quantum - Data Elements, Measures and Statistics*.

Kanavos, P. 2001. Communication of the European Communities, Dg. Enterprise. *Overview of Pharmaceutical Pricing and Reimbursement Regulation in Europe*. http://www.pharmacos.eudra.orf/F3/g10/docs/synthesis.pdf. April 2005.

Kravis, I.B. and Lipsey, R.E. 1969. "International Price Comparisons by Regression Methods." *International Economic Review*, 10:2, pp. 233-46.

Mossialos, E., Mrazek, M., and Wally, T. eds. 2004. *Regulating Pharmaceuticals in Europe: Striving for Efficiency, Equity and Quality*: Open University Press. European Observatory on Health Systems and Policies Series.

Mrazek, M. 2002. "Comparative Approaches to Pharmaceutical Price Regulation in the European Union." *Croatian Medical Journal*, 43:4, pp. 453-61.

Oaxaca, R. 1973. "Male-Female Wage Differentials in Urban Labor Markets." *International Economic Review*:14, pp. 693-709.

OECD. 2000. "Competition and Regulation Issues in the Pharmaceutical Industry." *Committee on Competition Law and Policy. Directorate for Financial, Fiscal and Enterprise Affairs: DAFFE/CLP(2000)29*.

OECD, H.D. 2003. "A Comparative Analysis of 30 Countries."

Pammolli, F., Riccaboni, M., and Magazzini, L. 2004. *European Competitiveness in Pharmaceuticals*.

Scherer, F.M. 1993. "Pricing, Profits and Technological Progress in the Pharmaceutical Industry." *The Journal of Economic Perspectives*, 7:3, pp. 97-115.

Scherer, F.M. 2000. "The Pharmaceutical Industry." *Handbook of Health Economics*, 1.
Seget, S. 2003. *Pharmaceutical Pricing Strategies: Optimizing Returns Throughout R&D and Marketing*. Reuters Business Insight - Healthcare.

Sirmans, G.S., Macpherson, D.A., and Zietz, E.N. 2005. "The Composition of Hedonic Pricing Models." *Journal of Real Estate Literature*, 13:1, pp. 3-43.

The Association of the British Pharmaceutical Industry. 2007. *Parallel Trade in Medicines*.

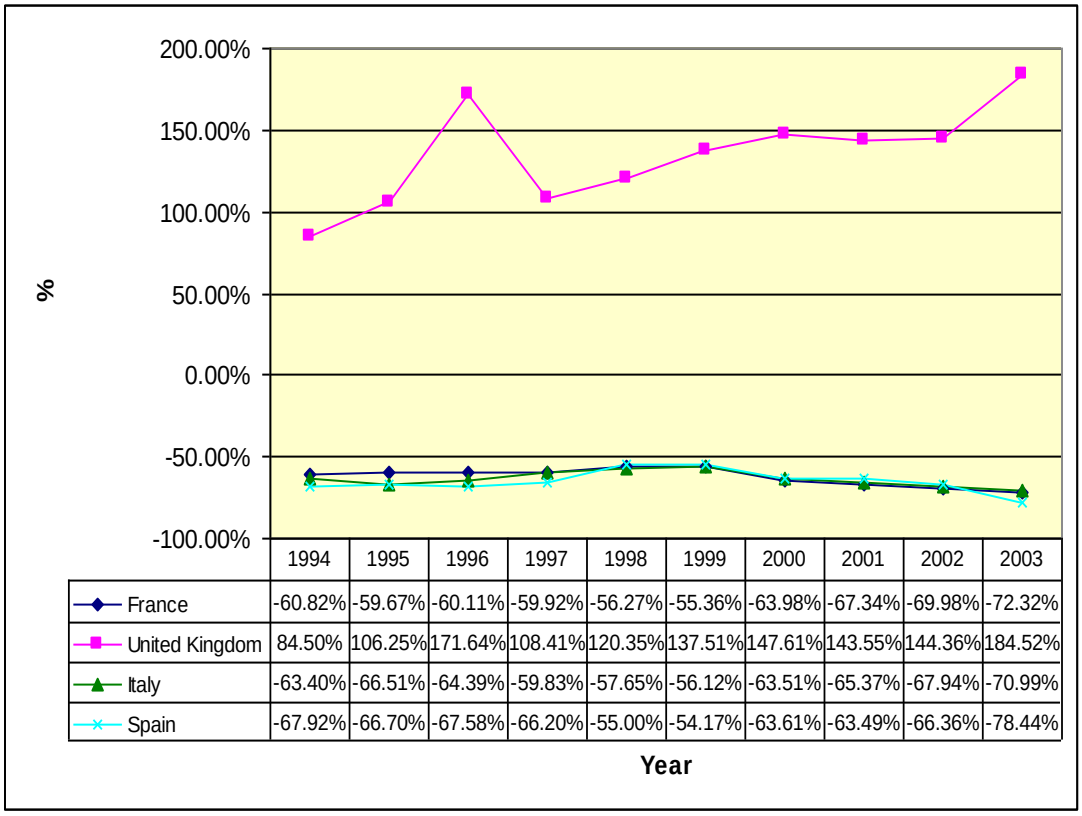
Towse, A. 1998. "The Pros and Cons of a Single "Euro-Price" for Drugs." *Pharmacoeconomics*, 13:3, pp. 271-76.

Table 1: Summary statistics

Variable	Germany	France	United Kingdom	Italy	Spain	Overall
SU Price (Local Euro)	0.6050 (2.1543) [0.2739] 957	0.2530 (0.2288) [0.0175] 581	1.3631 (4.8325) [1.5496] 587	0.2469 (0.1866) [0.0425] 683	0.2392 (0.3734) [0.0447] 616	0.5380 (2.3451) [1.1629] 3424
Molecule Age	21.3416 (15.3062) [2.8737] 1010	19.1308 (12.2691) [2.8745] 650	21.6077 (18.9893) [2.8745] 650	21.2161 (14.8060) [2.8741] 810	18.3082 (11.7177) [2.8743] 730	20.4112 (14.8796) [5.9994] 3850
Strength(g)	0.1614 (0.5469) [0.0326] 957	0.1664 (0.5254) [0.0052] 581	0.1359 (0.5210) [0.1390] 587	0.1368 (0.4569) [0.0485] 683	0.2309 (0.8002) [0.0177] 616	0.1655 (0.5783) [0.2525] 3424
Form Code	11.9132 (17.4706) [3.8606] 1060	2.5806 (2.5730) [1.0087] 670	7.0308 (9.9788) [2.7827] 650	2.5210 (2.6399) [1.0538] 810	2.7055 (3.4858) [1.0172] 730	5.8531 (10.9513) [8.8857] 3920
Pack Size	84.7394 (32.0237) [10.0290] 957	34.1315 (13.4550) [2.9280] 581	78.3298 (128.5843) [76.0274] 587	28.1088 (9.8395) [2.2096] 683	42.7100 (18.2813) [3.9063] 616	56.1955 (61.7375) [54.7582] 3424
Diffused Molecules	2.9859 (1.7320) [0.5446] 1060	3.7015 (1.6286) [0.5932] 670	3.8369 (1.5606) [0.5872] 650	3.4617 (1.6630) [0.5950] 810	3.6480 (1.6010) [0.5850] 730	3.4709 (1.6778) [0.5780] 3920
Generic Competition	7.6972 (11.3757) [3.5170] 1060	2.3328 (3.0771) [1.7684] 670	2.1169 (2.9040) [0.9818] 650	2.4383 (3.1272) [1.1564] 810	2.9781 (4.8973) [1.9443] 730	3.8895 (7.0646) [5.8167] 3920
Therapeutic Substitute Molecule	21.7604 (7.8990) [1.5810] 1060	15.0910 (4.8628) [1.2417] 670	13.1923 (4.0378) [1.2879] 650	15.1136 (5.2438) [1.5217] 810	15.1849 (6.1544) [1.3078] 730	16.6018 (6.8313) [4.1381] 3920

Each cell contains the mean in the top row, unconditional standard deviation in parentheses in the second row, within-molecule standard deviation in brackets in the third row, and number of observations in the bottom row.

Table 2: Fixed Local Euro Standard Unit (SU) Prices, Normalized to Germany



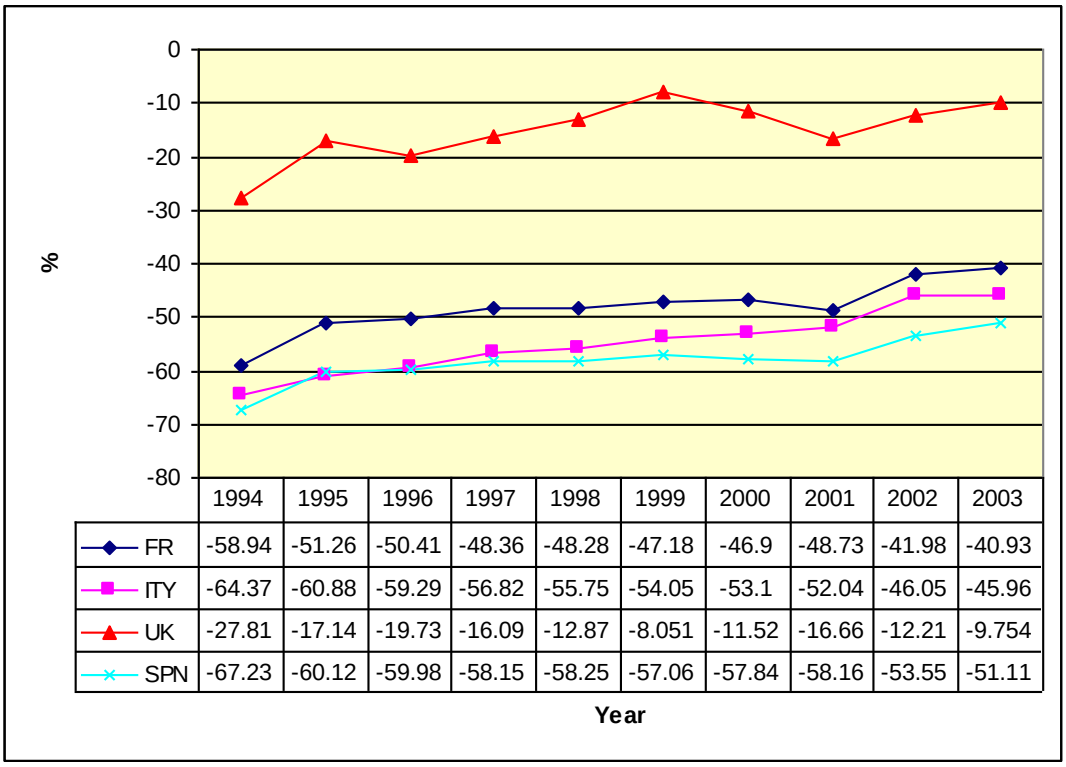
	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003
France	-60.82%	-59.67%	-60.11%	-59.92%	-56.27%	-55.36%	-63.98%	-67.34%	-69.98%	-72.32%
United Kingdom	84.50%	106.25%	171.64%	108.41%	120.35%	137.51%	147.61%	143.55%	144.36%	184.52%
Italy	-63.40%	-66.51%	-64.39%	-59.83%	-57.65%	-56.12%	-63.51%	-65.37%	-67.94%	-70.99%
Spain	-67.92%	-66.70%	-67.58%	-66.20%	-55.00%	-54.17%	-63.61%	-63.49%	-66.36%	-78.44%

Table 3: Quasi-Hedonic Price Regression Results

	Fixed Effects	Random Effects
Quality Characteristics		
ln Strength	0.3014 (0.0992)*	0.2160 (0.0666)*
ln Molecule Age	0.0113 (0.0846)	-0.2031 (0.0614)*
ln Form Code	-0.0406 (0.0539)	0.0653 (0.0502)
ln Pack Size	-0.4104 (0.0772)*	-0.3934 (0.0659)*
ln Diffused Molecules	-0.3651 (0.0830)*	-0.1870 (0.0886)**
Market (Competition) Characteristics		
ln Generic Competition	-0.0414 (0.0331)	-0.0608 (0.0279)**
ln Therapeutic Substitute Molecule	0.0615 (0.1009)	0.0623 (0.1098)
ln Therapeutic Substitute Molecule Entry Lag		0.1103 (0.1544)
Country dummies	Yes [0.0000]	Yes [0.0000]
Time dummies	Yes [0.0136]	Yes [0.0000]
Country/Time interactions	Yes [0.0000]	Yes [0.0000]
ATC Dummies	No	Yes [0.0000]
N	3,263	2,480
R^2 (Within)	0.4078	0.3689

The dependent variable is the log of the SU euro price. Parentheses contain standard errors that are robust to heteroskedasticity and are adjust for clustering by molecule. Brackets contain p-values of joint F-statistics. *, ** and *** reflect significance at the 1%, 5% and 10% levels, respectively.

Table 4: Quality Adjusted Bilateral (Country vs. Germany) Price Differences (%), Normalized to Germany



	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003
FR	-58.94	-51.26	-50.41	-48.36	-48.28	-47.18	-46.9	-48.73	-41.98	-40.93
ITY	-64.37	-60.88	-59.29	-56.82	-55.75	-54.05	-53.1	-52.04	-46.05	-45.96
UK	-27.81	-17.14	-19.73	-16.09	-12.87	-8.051	-11.52	-16.66	-12.21	-9.754
SPN	-67.23	-60.12	-59.98	-58.15	-58.25	-57.06	-57.84	-58.16	-53.55	-51.11

Table 5: Net Implicit Price Elasticities for Characteristics, 1994 & 2003
(*p*-values in parentheses)

Quality/Market Characteristics	Year	Germany	France	U.K.	Italy	Spain
Strength	1994	0.3023*	0.2678*	0.3071*	0.2487*	0.3073*
		(0.0000)	(0.0004)	(0.0020)	(0.0022)	(0.0017)
	2003	0.2560*	0.2441*	0.4453*	0.2527*	0.3221*
		(0.0004)	(0.0005)	(0.0000)	(0.0035)	(0.0011)
Molecule Age	1994	0.1248	-0.1784*	0.0013	-0.1709*	-0.2552*
		(0.190)	(0.0038)	(0.4035)	(0.0045)	(0.0000)
	2003	0.0894***	-0.0923**	-0.0176	-0.0427**	-0.3228*
		(0.0668)	(0.0163)	(0.6874)	(0.0178)	(0.0000)
Form Codes	1994	-0.0987	0.1765***	0.0520	0.2487**	0.2460*
		(0.222)	(0.0878)	(0.3541)	(0.0260)	(0.0061)
	2003	-0.1430	0.0931	-0.0554	0.2474*	0.2586*
		(0.2833)	(0.1370)	(0.4672)	(0.0060)	(0.0046)
Diffused Molecules	1994	0.1160	-0.3664	-0.9221**	-0.3000**	-0.0645
		(0.222)	(0.1511)	(0.0134)	(0.0453)	(0.4265)
	2003	-0.0819	-0.1931	-0.7649**	-0.3622**	-0.1048
		(0.1206)	(0.1086)	(0.0108)	(0.0178)	(0.2324)
Packsize	1994	-0.3605*	-0.6541*	-0.3960*	-0.4454*	-0.2347*
		(0.001)	(0.0000)	(0.0000)	(0.0001)	(0.0016)
	2003	-0.5677*	-0.4504*	-0.4560*	-0.5527*	-0.3676*
		(0.0002)	(0.0000)	(0.0000)	(0.0000)	(0.0002)
Generic Competition	1994	-0.1240**	0.0273	-0.1858**	-0.0248	0.0225
		(0.039)	(0.1074)	(0.0412)	(0.1165)	(0.1164)
	2003	-0.1305**	-0.0378**	-0.1841**	-0.1892*	-0.0969*
		(0.0121)	(0.0284)	(0.0154)	(0.0041)	(0.0096)
Therapeutic Substitute Mol.	1994	0.2718***	0.0025	0.0929	-0.2447**	-0.1954
		(0.084)	(0.1817)	(0.2214)	(0.0562)	(0.1003)
	2003	0.5084**	0.1468	-0.3557**	0.0766**	-0.2204**
		(0.0520)	(0.1231)	(0.0318)	(0.0139)	(0.0269)

*, ** and *** reflect $p<0.01$, $p<0.05$ and $p<0.10$

Table 6: Decompositions-Explained (Average Characteristics) vs. Unexplained (Implicit Price Effect)										
FRANCE vs. GERMANY	**1994**	**1995**	**1996**	**1997**	**1998**	**1999**	**2000**	**2001**	**2002**	**2003**
Explained										
Quality	0.5298	0.4530	0.4195	0.4742	0.5244	0.5456	0.6179	0.6236	0.6258	0.6904
Competition	0.0546	0.1419	0.1534	0.1060	0.0310	0.0018	0.0457	0.0318	0.0097	-0.0447
Unexplained	-1.0383	-0.9879	-0.9270	-0.8798	-0.8746	-0.8467	-0.9516	-0.9938	-1.0209	-0.9170
Total: Log of Observed Price Ratios	**-0.4539**	**-0.3929**	**-0.3542**	**-0.2996**	**-0.3192**	**-0.2993**	**-0.2880**	**-0.3384**	**-0.3854**	**-0.2712**
ITALY vs. GERMANY										
Explained										
Quality	0.4941	0.4361	0.4280	0.4781	0.5831	0.5924	0.7041	0.7078	0.7325	0.8313
Competition	0.0202	0.0980	0.1096	0.0792	0.0252	0.0466	0.0544	0.0364	0.0276	-0.0400
Unexplained	-1.1975	-1.2192	-1.1387	-1.0736	-1.0629	-1.0364	-1.1344	-1.0853	-1.0269	-1.0307
Total: Log of Observed Price Ratios	**-0.6831**	**-0.6851**	**-0.6011**	**-0.5162**	**-0.4546**	**-0.3974**	**-0.3758**	**-0.3411**	**-0.2668**	**-0.2394**
U.K. vs. GERMANY										
Explained										
Quality	0.0578	-0.1388	-0.1181	-0.0215	0.0212	0.0788	0.2200	0.2329	0.2433	0.2745
Competition	0.0048	0.1109	0.1094	0.0660	0.0005	0.0235	0.0215	-0.0141	-0.0044	-0.0498
Total Unexplained	-0.2252	-0.1286	-0.1774	-0.1047	-0.0856	0.1400	0.0807	-0.0048	-0.3506	0.1012
Total: Log of Observed Price Ratios	**-0.1626**	**-0.1565**	**-0.1861**	**-0.0603**	**-0.0639**	**0.2423**	**0.3221**	**0.2141**	**-0.1117**	**0.3259**
SPAIN vs. GERMANY										
Explained										
Quality	0.4881	0.4111	0.3813	0.4450	0.5324	0.5532	0.6144	0.6234	0.6172	0.6818
Competition	0.0151	0.0815	0.0968	0.0618	0.0196	0.0286	0.0154	-0.0117	-0.0163	-0.0833
Total Unexplained	-1.2050	-1.1665	-1.1111	-1.0310	-1.0922	-1.0557	-1.1155	-1.1158	-1.0585	-0.9740
Total: Log of Observed Price Ratios	**-0.7017**	**-0.6739**	**-0.6330**	**-0.5242**	**-0.5401**	**-0.4739**	**-0.4856**	**-0.5040**	**-0.4576**	**-0.3755**

Appendix Table A-1: Selected EU National Health Care Systems, Demand and Supply Side Regulations				
	SUPPLY-SIDE			DEMAND-SIDE
CTRY:	**NATIONAL HEALTH CARE SYSTEMS**	**PRICING**	**REIMBURSEMENT**	**PRESCRIBING, DISPENSING AND CONSUMPTION**
GR	**The Statuary Health Insurance and Private Insurance.** REGULATORY APPROACH[1]: **Free pricing:** -Applies to in-patent drugs -Doesn't apply to multi-sourced drugs[2] -Doesn't apply to OTC	Price freedom for new products (since 1995)	a) Reference price for off-patent sector (1989) b) Drug budgets (re-introduced 1999) c) Negative list (1983) d) Positive list (since 2001)	a) Negative list (1983) b) Budget (Funded by National) c) Guidelines/Monitoring d) Generic Prescribing e) Substitution f) Incentives g) Co-Payment: Flat fee per pack
UK	**The National Health Service** REGULATORY APPROACH: **Cost-Effectiveness Pricing and Profit Controls:** -Applies to in-patent drugs -Doesn't apply to multi-sourced drugs -Doesn't apply to OTC	a) Agreement with industry on profit control b) Price cut (4.5%) c) Free price modulation by 2001 d) "Maximum Price Scheme" for generics (2000)	a) Negative list b) Practice and prescribing guidelines	a) Negative list b) Budget (Funded by National) c) Guidelines/Monitoring d) Generic Prescribing e) Incentives f) Co-payment: Flat fee per item
FR	**The Statuary Health Insurance** REGULATORY APPROACH: **Fixed Pricing and Cost-Effectiveness Pricing:** -Applies to in-patent drugs -Applies to multi-sourced drugs -Doesn't apply to OTC	a) Price fixing through negotiation b) Comparisons with other European countries for "innovative" products c) Periodic price reductions for new and expensive products d) Price freedom has been introduced since 2003	a) Committee decides on reimbursable prices on advice from Transparency committee b) Positive list c) Medical references d) Targets for "gate-keeping" (General Practitioners) e) Pharmacoeconomic guidelines under development f) Prices of generics 30% lower than original (1998)	a) Positive list b) Budget (Funded by National) c) Guidelines/Monitoring d) Generic prescribing e) Substitution f) Incentives g) Co-payment: % (0, 35, 65)
ITY	**The National Health Service** REGULATORY APPROACH: **Fixed Pricing and Cost-Effectiveness Pricing:** -Applies to in-patent drugs -Doesn't apply to multi-sourced drugs -Doesn't apply to OTC	a) Average European Price (EU countries) for "old" products and products registered with the national procedure (Altered: 1998) b) Price negotiation (contractual model) for new and innovative products c) Price freedom for non-reimbursable drugs d) Generics are priced at least 20% below the original e) Frequent use of price cuts/freezes	a) Positive list b) Reference listing and same prices for same drugs' principle for off-patent drugs c) Formal requirement for economic evaluation during price negotiations d) Guidelines and protocols defined and managed at local level e) Official earmarked budget for innovative drugs introduced in 1998	a) Positive list b) Budget (Funded by Regional) c) Guidelines/Monitoring d) Substitution e) Co-payment: % (0, 50, 100) +flat fee
SPN	**The Statuary Health Insurance** REGULATORY APPROACH: **Fixed Pricing:** -Applies to in-patent drugs -Applies to multi-sourced drugs -Applies to OTC	a) Price control through negotiation on a cost-plus basis b) International price comparisons c) Price-volume agreement for expensive products	a) Positive list b) Negative list (1998) c) Reference pricing for estimating maximum reimbursement for multi-source products	a) Negative AND Positive list b) Guidelines/Monitoring c) Generic prescribing d) Co-payment: % up to a max. per item price (0, 10, 40)
Adapted from (Kanavos 2001) and compiled from (Seget 2003), (Mossialos, et al. 2004)				

[1] Summary of general approach to regulation of pharmaceutical prices, (Mrazek 2002).
[2] Brand name drugs that have generic equivalents.