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EFFECTS OF REGULATION ON DRUG LAUNCH AND PRICING IN INTERDEPENDENT MARKETS

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ABSTRACT

This study examines the effect of price regulation and competition on launch timing and pricing of new drugs. Our data cover launch experience in 15 countries for drugs in 12 therapeutic classes that experienced significant innovation over the decade 1992-2003. We use prices of established products as a measure of the direct effect of a country's own regulatory system, and find that launch timing and prices of innovative drugs are influenced by prices of established products. Thus, if price regulation reduces drug prices, it contributes to launch delay in the home country. New drug launch hazards and launch prices in low-price countries are also affected by referencing by other, high-price countries, especially within the EU, as expected if manufacturers delay launch in low-price markets to avoid undermining higher prices in other countries. Thus, referencing policies adopted in high-price countries can impose welfare loss on low-price countries. Prices of new drugs are influenced mainly by prices of other drugs within the same subclass; however, dynamic competition from new subclasses undermines new drug launch in older subclasses. Association with a local firm accelerates launch only in certain regulated markets. These findings have implications for US proposals to constrain pharmaceutical prices in the US through external referencing and drug importation.

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I. Introduction

New drugs are potentially global products and can contribute importantly to health outcomes for consumers and expenditures for payers. Prompt launch is also critical for drug manufacturers, given the fixed patent life over which to recoup the high costs of R&D.[1] In fact, in a study of the 1990s launch experience of 85 drugs in 25 industrialized countries, only roughly half of the potential country-compound launches occurred, and many of the eventual launches involved months or years of delay (Danzon, Wang and Wang, 2005). Launch lags in the US in the 1960s and 1970s were attributed to increased regulatory requirements for proof of safety and efficacy (e.g. Peltzman, 1973; Grabowski and Vernon, 1978). However, in the 1990s the US and the EU harmonized and accelerated new drug review, such that remaining differences in registration requirements cannot fully explain observed launch lags, especially between EU countries.

By contrast, price regulation has become more complex and potentially contributes both direct (domestic) effects on launch lags in the regulating country and indirect (spillover) effects on launch in other countries. Price regulation may delay launch directly through three mechanisms. First, regulation that reduces the manufacturer's expected price and NPV reduces incentives for launch, especially in small countries and for drugs with low expected sales volume, assuming some fixed costs of launch. Second, negotiation strategies may lead to strategic delay by firms or regulators to influence the ultimate price.[2] Third, regulatory processes may entail pure bureaucratic delay. The welfare consequences of these direct/domestic effects of a country's regulation on its citizens are ambiguous *a priori*, because any foregone health benefit

[1] Pharmaceutical R&D takes on average 8-12 years and costs roughly $802m. (in 2001 US dollars) per new compound approved in the US (DiMasi, Hansen and Grabowski, 2003).
[2] Delay could also reflect launch budget constraints faced by firms, in which case a rational strategy may be to launch first in the most profitable markets and use the revenues generated to cover launch in less profitable markets.

due to fewer/later launches may be offset by savings from lower drug prices and better pre-launch information about a drug's relative safety and effectiveness.[3]

More problematic from a social welfare perspective are the indirect/spillover effects that arise when one country regulates its drug price by reference to the price of the same drug in other countries ("external referencing"). For example, Canada caps the price of innovative new drugs at the median price in seven countries, and some EU countries use the mean or minimum price in a group of referenced countries. By undermining market segmentation and price discrimination, external referencing by high-price countries creates spillover incentives for a firm to not launch in lower-price referenced countries or delay until a higher price is achieved. The welfare consequences in the referenced low-price countries are clearly negative, since they suffer reduced access to new drugs and possibly higher prices due to external referencing by other countries, with no offsetting benefits. Parallel importation by high-price EU countries from lower-price EU countries is a second spillover mechanism that may also contribute to non-launch and higher prices, and hence negative welfare consequences for the exporting countries.[4] Understanding these indirect effects of one country's regulation on launch in other countries is particularly important as existing regulatory regimes seek new ways to constrain drug prices and the US debates both referencing foreign drug prices and/or legalizing parallel trade ("drug importation").

Previous studies of launch experience for new drugs (Danzon, Wang and Wang, 2005; Lanjouw, 2005; Kyle, 2006, 2007) have generally concluded that price regulation contributes to

[3] Negative external effects may accrue to other countries if the regulated prices result in suboptimal contribution to joint costs of R&D (Danzon and Towse, 2003).

[4] Parallel trade is expected to have less effect on launch delay in low-price countries than external referencing because (a) parallel trade only reduces prices for the traded fraction of sales, (b) manufacturers may be able to limit parallel trade supply restrictions to exporting countries, two-tier price structures etc., and (c) launch delay would simply delay the onset of trade with no lasting effect on post-launch price differentials.

launch delay. As detailed below, however, these prior estimates are inconclusive because: their proxy measures of regulation were at best rough and sometimes inaccurate, leading to possible measurement error and some contradictory results; they lacked product-specific data on prices of competitor products, a critical benchmark for regulation and hence expected launch prices; they estimated launch equations that presupposed regulatory effects on launch prices, but were unable to corroborate with evidence on launch prices; and none clearly distinguished the indirect spillover effects of regulation from benign determinants of launch sequencing.

This paper provides robust estimates of the effects of regulation on both launch delay and launch prices. We distinguish clearly between the direct/domestic effects of a country's own regulatory system and the indirect/spillover effects on other countries, and clarify the negative welfare consequences of the spillover effects. We use the average price (lagged one quarter) of established products in the same subclass as the most accurate available measure of the effect of regulation on expected prices and hence the direct effect of regulation on launch.[5] We distinguish the influence of products in the same vs. older subclasses, to provide evidence on whether the availability of older, cheaper products constrains launch prices for new drugs in innovative

[5] We treat the lagged average price of competitor products as exogenous because prices are regulated in all but three countries in our sample; the exceptions are the US, Germany (except classes under reference pricing and time periods with price freezes) and the UK (except price increases are not permitted). Although firms could in theory cut price below the regulated price, this would not be a rational entry deterrence strategy in pharmaceutical markets for two reasons. First, subsequent price increases would be barred by regulation, and, second, patients have little incentive to be price-sensitive in most markets, because co-payments are generally independent of drug price. To check the assumption that prices are sticky and are unrelated to anticipated launch of competitors, we compared several measures of price change (all measured as percents) prior to launch with price change in other periods. Median price change within subclasses is zero, whether measured quarterly or annually, and the 5th and 95th percentiles are -6.2 and 6.3 respectively. For superior drugs, a launch occurred in roughly 10 percent of quarters. The 10th percentile of annual price changes was -7.2 for years prior to a superior launch vs. -8.6 for periods with no superior launch; patterns are similar for all other percentiles and for inferior drugs. Focusing on superior subclasses where preemptive price cutting is most plausible, the 10th percentile of the overall 4-quarter change is -10.4 for subclasses with 3 or fewer competitors vs. 7.7% for subclasses with more than 3 competitors. In subclasses with 3 or fewer competitors, the 10th percentile of the 4-quarter price change for years prior to entry is -7.5 vs. other years is -10.9. Because lagged competitor prices are set by regulation and do not plausibly reflect strategic entry deterrence, these prices provide a much more accurate, composite measure of the net effect of complex regulatory regimes on the expected price for a new drug than the alternative of including binary indicators for regulatory regime structural type, which cannot capture the complex and multidimensional details of regulatory implementation, including unobserved processes that vary widely within structural type.

subclasses and hence the extent of static vs. dynamic competition. We also provide evidence on (lack of) first-mover advantage and differential country-specific influence of local corporations.

We analyze quarterly sales data, by drug, from IMS Health from 1992-2003 for 15 major countries and 12 major therapeutic classes, all of which experienced entry of a new subclass during our study period (e.g., in the anti-ulcerant class, the proton pump inhibitors [PPIs] displaced the H2-antagonists). We refer to new and old subclasses as "superior" and "inferior," but intend no judgment about their relative value.

We estimate a two-equation model of launch hazard and launch price for molecules in superior and inferior subclasses separately, to permit comparison between them. The launch hazard equation is estimated using a complementary log-log (hereafter "clog-log") model with time-varying covariates. We also estimate a random effects clog-log model and a split population clog-log model (Schmidt and Witte, 1989) to test for various forms of molecule-level heterogeneity. The launch hazard results are robust to specification, although both the split population and the random effects hypotheses are confirmed. For the launch price equation, we report estimates of price conditional on launch from OLS and GLS random effects models. We test for selection bias, using a two-step Heckman selection estimator (Heckman, 1979). Although the inverse Mills' ratio is sometimes significant, the launch price results are also robust to specification.

We find that launch hazards and prices of new drugs are positively associated with prices of established products in the same subclass, but find no evidence of effects of old subclasses on new subclasses. Thus, to the extent that regulation reduces drug prices, it directly contributes to launch delay/non-launch, but availability of older, cheaper drugs does not constrain new drug prices. Regulatory referencing by high-price EU countries contributes to launch delay/non-

launch in low-price EU countries. We find no evidence that manufacturers use delay as a strategy to obtain a higher price within a given country. Launch by local corporations accelerates launch timing but does not affect launch prices; these effects are confined to a few, regulated countries, however, suggesting local firms benefit from political influence rather than real experience advantages. Late-launching drugs in older subclasses have more limited launch success than new drugs in new subclasses, confirming the importance of non-price dynamic competition.

The evidence here shows that indirect regulatory strategies that rely on referencing to foreign prices or importing from foreign countries can impose significant welfare loss on these foreign countries due to launch lags, non-launch and higher prices.[6] The model implies that such effects will be greater, the larger the referencing country relative to the referenced country and the greater the potential price difference. Thus, this evidence is particularly relevant as the US considers external referencing and/or legalizing drug importation/parallel trade, given the huge size of the US market (45 percent of global pharmaceutical sales) relative to potential referenced countries.[7] It is also relevant to the growing concern over high prices of drugs in developing countries, which are plausibly attributable in part to the risk of referencing or importation by higher-priced countries, as well as other factors.

[6] Estimating the magnitude of welfare consequences of regulation is beyond the scope of this paper. Philipson et al. (2008) estimate the welfare effects of launch delay due to registration regulation in the US. In their model, registration regulation is assumed to reduce drug risk but delay consumer access to drug benefits, which are measured by actual drug prices. By contrast, our focus is on launch delay due to price regulation. The presumption of price regulation is that unregulated consumer demand is not a valid measure of consumers' marginal benefits from drugs when consumers face minimal or zero out-of-pocket payment, as in most countries. If consumer demand for a drug is highly inelastic due to low/zero co-payment, but consumers ultimately must pay the full price through taxes or insurance premiums, then regulation that constrains prices to reflect the "true" value of drugs can increase consumer welfare in that country. Of course, if regulators set prices below the true value of new drugs to consumers, there may be long-run negative consequences due to reduced R&D.

[7] As of February 2009, regulating US prices based on external referencing to foreign prices has been proposed but so far not enacted. Drug importation has been approved but so far is not implemented, because the Secretary of Health and Human Services has been unwilling to certify that safety and cost reduction requirements would be met. Several new bills would relax these constraints and expand the set of exporting countries.

The remainder of the paper is organized as follows. Section II reviews the relevant literature, Section III outlines regulatory regimes and expected effects, and Section IV describes the theoretical model. Section V details the data and empirical methods, Sections VI-VIII describe the results, and Section IX concludes.

II. Literature

Several recent studies have examined effects of price regulation on lags in new drug launch. Danzon, Wang and Wang (2005) studied the launch experience of 85 new drugs in the 25 leading markets in the 1990s, focusing on drugs that had met registration requirements of one of the two strictest agencies (the US Food and Drug Administration [FDA] and the UK Medicines Agency) and hence could potentially meet registration requirements in other countries. This analysis used as a proxy for the direct regulatory effect on a new drug's expected price the average price of *all* competitor products in the class, *measured at the time of the new drug's global launch*. This class-wide average price at global launch may be an imprecise measure of expected price for launches in a new subclass. For example, consider the launch of the third proton pump inhibitor (PPI), a subclass within the broad anti-ulcerant class. The Danzon et al. (2005) analysis used the class-wide average price of all anti-ulcerants, including many older, off-patent products with modest efficacy, measured at global launch which may be many months before actual launch. By contrast, our present study estimates separate effects of (a) the average price of other brand PPIs ("superior" brands) vs. (b) the average price of older brands in other anti-ulcerant subclasses ("inferior" brands), and (c) the average price of generics, all measured contemporaneously (one quarter prior to launch). We find that launch of new brands is affected only by prices of brands in the same subclass. That prices of new drugs are not constrained by

prices of older, cheaper originator or generic substitutes has important implications for regulatory policy.

Kyle (2007) used a more heterogeneous sample of compounds and countries, a longer time period (1980-1999), and measured regulation with a vector of regulatory structure indicators and a price rank indicator.[8] She concluded that price controls reduced launch probability in countries that impose them. However, this conclusion is unreliable given the many limitations of her measures of regulation. The regulatory indicators from 2000/2002 postdate the 1980-1999 analysis period and do not reflect significant changes in several countries within the analysis period. The indicators incorrectly classify some countries and are missing for others.[9] More fundamentally, within each measured regulatory type, there are major unmeasured differences across countries and over time that affect prices. Kyle's only measure of expected price is an indicator for a country's price rank in 2002, which is invariant across classes and years. This was negatively related to launch probability prior to 1995, contrary to predictions, and insignificant after 1995.[10] Kyle's (2006) analysis of launch in the G7 countries uses a single

[8] The large and heterogeneous sample probably includes some drugs that could not meet requirements of the strictest agencies, such as the US FDA, the UK Medicines Agency and the EMEA. A count of Medline citations is included as a control for product quality; however, this US-centric measure may be a biased proxy for quality as perceived by non-US countries, especially for drugs not launched in the US.

[9] Several examples illustrate the measurement error that results from applying the 2000/2002 listing of regulatory indicators to the 1980-1999 data. In the paper, "price controls refer to a cap on either the ex-manufacturer price or the amount a national health service pays for a pharmaceutical product." By this definition, therapeutic reference pricing should count as a form of price control, because the reference price is a cap on reimbursement for all drugs in a class. In fact, therapeutic reference pricing is included as a separate dummy variable and has a coefficient that is positive and sufficiently large (0.854) to dominate the negative price control coefficient (-0.418). But, this effect appears to be spurious due to measurement error: although 7 countries are classified as having therapeutic reference pricing, in fact only the Netherlands had comprehensive therapeutic referencing, and this was only introduced in 1991. Similarly, 6 countries are categorized as "Pharmacoeconomic evidence recommended," but in fact pharmacoeconomic evidence was used informally to support price negotiations in many countries from the early 1990s. In the late 1990s, both the UK and Canada required pharmacoeconomic evidence, but neither of these countries are categorized recommending use of pharmacoeconomic evidence. Given this measurement error, the large negative coefficient on this variable is unlikely to provide an accurate measure of the effect of requiring pharmacoeconomic evidence. Germany is listed as having a Prescribing budget, but in fact it was only in place from 1993-2000, and never enforced.

[10] The post-1995 interaction alone is significant but when combined with the main effect, the net effect appears to be insignificant. High (1%) significance levels for most explanatory variables are surprising and may be upward biased

binary indicator for drug price controls. This is negatively associated with launch probability in some specifications, but is insignificant in others. Thus this evidence for the direct effects of regulation on launch probabilities from these analyses using regulatory indicators is inconclusive.

With respect to spillover effects of regulation, all prior papers use indicator variables for prior launch in a high-price vs. low-price country. However, none tests for differential effects between countries that are closely linked vs. those that are not, which is necessary to distinguish regulatory spillovers from other unobserved factors that may lead to sequenced launches, such as coordinated regulatory filings. Finally, all prior papers show that launch by a local corporation increases launch probabilities on average, but there is no analysis of differential effects across countries and no compelling evidence on whether this reflects a true experience advantage or simply political bias towards local firms.

Lanjouw (2005) examined first launch in a large, heterogeneous sample of new drugs in 68 countries between 1982 and 2002, using covariates measured at first global launch. She also lacked data on competitor prices and measured regulatory stringency with binary indicator variables that are invariant across classes and over the 20-year study period. Given the imprecise measure of regulation, the conclusions on direct effects of price regulation are inconclusive.[11] Lanjouw did not address spillover effects.

None of the previous papers examine effects of regulation on launch prices. Kanavos and Costa-Font (2005) argue that parallel trade has led regulators in the lower-price EU countries, such as Italy, France and Portugal, to accept higher prices, but they do not directly test this.

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by including multiple indications for the same compound. Follow-on indications are usually not subject to price regulation and simply receive the same price as previous indications, with minimal price-related regulatory delay. Including follow-on indications could also bias coefficients and standard errors.

[11] Lanjouw concluded that price controls in high-income countries reduced the long-run likelihood of drug launch, while price controls in less wealthy countries reduced launch probability in the short-run but not the long-run.

Similarly, Grossman and Lai (2006) present a theoretical model in which regulators in parallel export markets accept higher regulated prices under regimes of international patent exhaustion, in which their low prices undermine R&D, but no empirical evidence is presented. Our paper is the first to provide evidence of effects of regulatory spillovers on launch prices.

III. Pharmaceutical Regulation: Registration and Price/ Reimbursement

New drugs face two possible regulatory hurdles: registration and price approval.

Registration

In all countries, drug registration requires proof of safety, efficacy and manufacturing quality as a condition of market access. In the 1990s, the US FDA and counterpart agencies in Europe harmonized some data requirements and adopted measures to accelerate review while retaining autonomy in decision-making. Since 1995, the newly-created European Medicines Agency has offered both centralized and mutual recognition procedures that can lead to simultaneous registration of new drugs in all EU countries, as an alternative to the traditional country-by-country review through national drug approval agencies.[12] Thus cross-national differences in drug registration regulation cannot explain large systematic differences in launch lags among EU countries or between the US and EU. Japan is an exception in retaining special requirements, including clinical trials on Japanese citizens.

Price/Reimbursement Regulation

Once a new drug clears registration hurdles, most countries with national health insurance systems require price approval as a condition of reimbursement.[13] Countries use one or

[12] Under the mutual recognition procedure, a manufacturer selects one rapporteur country to review the application; other countries have 90 days in which to challenge the approval, otherwise it takes effect automatically.
[13] Price approval is generally not required if the drug is launched without reimbursement, but such unreimbursed launch is rare, except for "lifestyle" drugs.

both of two criteria to set launch prices: (a) "internal referencing" to prices of one or more competitor products in the same therapeutic class, with potential for mark-ups for superior efficacy or other factors,[14] or (b) "external referencing" to the minimum, median or mean of prices of the same drug in specified comparator countries. Most price regulatory regimes disallow post-launch price increases, and price cuts are sometimes mandated; hence the launch price is critical to a drug's life-cycle price profile. Internal referencing may entail bureaucratic delay and possibly strategic delay if firms (regulators) hold out to achieve a higher (lower) price. However, regulators should have incentives to weigh any costs associated with launch delay against the benefits in lower prices, with no significant spillover to other countries.

By contrast, because external referencing regimes benchmark their price to the price of the same drug in other countries, they create incentives for firms to delay launch in referenced lower-price countries until prices have been established in other potentially higher-price countries and/or regulators in low-price countries accept higher prices. Thus, higher-price countries that reference lower-price countries can impose launch delay and possibly contribute to higher prices in the referenced countries.[15]

Identifying the contribution of these regulatory regimes to drug launch experience in specific countries is complex because most countries use multiple forms of regulation, including both internal and external referencing, and the details of each regulation type differ across

[14] Internal referencing may involve informal negotiations between the manufacturer and the regulator, as in France, or a more mechanistic reference price (RP) reimbursement system as in the Netherlands. Under therapeutic RP, drugs are classified based on mechanism of action and indication; generic RP groups drugs only with the same molecule, hence mainly off-patent drugs with generic equivalents. All drugs in a group receive the same reimbursement or reference price. A manufacturer may in theory charge a higher price, but the patient must pay any excess over the RP.

[15] For example, suppose that in the absence of referencing, drug prices would be roughly proportional to GDP per capita. If high-income countries reference the mean price in a group of lower-income countries, the low-income countries are likely to experience spillover launch delay and welfare loss. But if a low-income country references the minimum price in other middle and low-income countries, any launch delay and welfare loss experienced by the referring low-income country would be internalized. Thus, referencing is predicted to lead to delays in lower-price countries, regardless of who does the referencing, but effects are external to the regulator's calculus when higher-price countries reference lower-price countries.

countries. The effects of internal referencing depend on country-specific details, in particular, the choice of comparator products and criteria for and size of mark-ups, if any. External referencing effects depend on countries referenced, whether minimum, median or mean price is used, and the other countries that the referenced countries reference. The complexity of these regulatory details makes it impossible to accurately categorize countries by regulatory indicators or derive a firm's optimal launch sequence and minimum reservation price for each drug-country pair. However, a clear prediction is that referencing of low-price countries by high-price countries will exacerbate launch delay and possibly raise prices in the low-price countries.

Of the countries in our data during our study period, France, Japan, Canada, the Netherlands, Italy, Mexico and Brazil nominally used both internal and external referencing for some drugs and/or time periods.[16] Greece and Portugal also used externally referenced price controls for most of the period.[17]

In the US, Germany and the UK, a new drug could be launched and reimbursed without regulatory approval of price, although other control mechanisms applied. In the US, multiple private health plans negotiate discounts in return for preferred formulary status, and Medicaid requires discounts off the price charged to private payers. These mechanisms may influence launch prices but should not delay launch. Germany adopted an internal reference price reimbursement system in 1989 but excluded new on-patent drugs, which could be launched and

[16] Many other countries, including the UK, Sweden, Italy, Germany and Spain, and most US health plans used RP reimbursement for generically equivalent, off-patent compounds for at least part of our period. However, because these generic RP systems apply to off-patent drugs only, they are unlikely to affect launch decisions for new drugs, unless inter-brand effects are significant due to either competition or informal referencing.

[17] The EU countries that used external reference pricing include Denmark (since April 1997, up to 10 EU countries excluding Greece and Italy), Greece (lowest in the EU), Ireland (lower of UK or the average in Denmark, France, Germany, the Netherlands, and the UK), Italy (average of up to 12 EU countries, must be on market for 4 countries and at least 2 with direct price controls), the Netherlands (since June 1996, average price in Belgium, France, Germany, and the UK), and Portugal (lowest in France, Italy, and Spain) (Burstall, 1998).

reimbursed without price approval, until 2005.[18] The UK permits free pricing of individual drugs, subject to a rate of return constraint on each firm's portfolio of drugs. The renegotiation of this profit-control scheme every five years usually involves international price comparisons and required cuts in UK prices. Since 1999, the National Institute of Clinical Excellence (NICE) has reviewed cost-effectiveness as a condition of reimbursement for most new drugs, which could slow or prevent new drug launch.

The inability of regulatory indicator variables to accurately measure these complex regulatory systems is evidenced by results from international price comparisons. For example, although France, Japan and Canada all use both internal and external referencing, weighted price indexes for 1999 show Canadian and French prices roughly 30 percent lower than the US, whereas Japan's prices were over 20 percent higher than the US (Danzon and Furukawa, 2003). Rather than use regulatory type indicators, we therefore use average prices of competitor products as the most accurate measure of the net direct effect of each country's regulatory system on expected prices for new drugs. These lagged prices can be treated as exogenous, because prices are constrained by regulation in most countries and incentives for competitors to cut price as an entry deterrence strategy are weak or nonexistent (see footnote 5). We also categorize countries as high-price EU countries (UK, Germany, Netherlands, Sweden), low-price EU countries (France, Spain, Portugal, Italy, Greece), and high-price non-EU countries (US, Canada, Japan, Switzerland), based on average prices in our dataset and evidence from earlier price comparisons (Danzon and Furukawa, 2003).

Parallel Trade

[18] From 1993-2000 Germany had a national drug budget with physicians nominally at risk for budget overruns, although paybacks were not enforced. In 2005 on-patent drugs were added to the reference pricing system for reimbursement.

Parallel trade between EU states is legal under the Treaty of Rome. In our data, parallel imports are reported only in the high-price EU countries. Parallel exporting countries are mainly the low-price EU countries (France, Spain, Italy, Greece, and Portugal) (Burstall, 1998). Parallel export risk may raise a firm's reservation price for launch in low-price countries within the EU. Measurement of parallel trade risk is described below.

IV. Theoretical Model

If markets were separable and prices were unregulated, profit-maximizing firms would set prices independently for each country and would launch promptly after registration in all markets where the expected net present value of revenues exceeds country-specific fixed launch costs. With price regulation and potential spillovers, a necessary condition for launch of drug *s* in country *j* is that expected net present value of revenues exceeds country-specific fixed costs plus any revenue loss in other countries due to spillovers:

$$\int_{t=1}^{T}\left\{\left[P_{sjt}\left(P_{bjt}(R),P_{gjt}(N_{gjt}),Y_j;P_{skt}\right)-C_{sjt}\right]\times Q_{sjt}\left(Q_{jt},N_{bjt},N_{gjt}\right)-\sum_{k\neq j}X_{jkt}\left(P_{sjt},R_{kt},I_{kt}\right)\right\}e^{-rt}dt > F_{jt}(H) \qquad (1)$$

The expected price of product *s,* $P_{sjt,}$ is assumed to depend on: P_{bjt}, the average price of competitor brand products, which depends on regulatory regime *R;* the average price of competitor generics P_{gjt} which depends on number of generic competitors N_{gjt}; per capita income, *Y,* which may affect demand and regulatory stringency; and $P_{skt,}$ the price of drug *s* in countries $k\ldots K \geq 0$ that are referenced by *j.* Expected sales volume Q_{sjt} depends on aggregate sales in the class Q_{jt}, and on the number of brand and generic competitors N_{bjt} and N_{gjt}.[19]

[19] Footnote 5 explains why we treat average price of branded competitor products P_{bjt} as exogenous. Number of brand competitors was never significant and was dropped. We treat number of generic competitors in the class as exogenous because generics can only enter into older, off-patent molecules, and generics are substituted mainly within these older molecules. Generic entry also requires regulatory approval, which can take several years.

Expected net revenue from launch is decreasing in $X_{jk} = \partial(P_k Q_k)/\partial P_{sj}$, the spillover effect of P_{sj} on revenues in country k, which either references to j or derives parallel imports I from j. $F_j = F_R + F_P$ is total fixed cost of drug launch, including registration cost F_R and price approval cost F_P, which may be lower if the launching corporation is home-based H; T is the duration of the economic life of the drug indexed by t; and r is the discount factor.

Equation 1 yields the firm's reservation price for launch in country j. It is increasing in X_{jk} if launch in j may reduce revenue loss in country k due to spillovers from country j ($\partial P_{sj}^{Ask}/\partial X_{jk} > 0$). If F is invariant across countries and drugs, reservation price is decreasing in expected market size ($\partial P_{sj}^{Ask}/\partial Q_{sj} < 0$). More generally, firms are less likely to launch drugs in countries with low expected sales, due to low volume or because price regulation reduces expected prices.

The regulator's reservation or maximum offer price depends on the regulatory regime. Under internal referencing, the regulator's offer depends directly on prices of substitute products ($\partial P_{sj}^{Offer}/\partial P_{bj} > 0$). Under external referencing, although the regulatory formula is based on prices in comparator countries, prices of existing products provide an empirical proxy for achievable price levels under the referencing formula. Regulatory offers may be related to per capita income ($\partial P_{sj}^{Offer}/\partial Y_j \geq 0$), given the political pressures on regulators to constrain health spending within budgets that are related to per capita income levels. Budget impact may lead regulators to offer lower prices for drugs with relatively large potential volume, Q_{sj}, other things equal ($\partial P_{sj}^{Offer}/\partial Q_{sj} \leq 0$). If local corporations are favored, $\partial P_{sj}^{Offer}/\partial H_j \geq 0$.

If $P_{sj}^{Offer} - P_{sj}^{Ask} \geq 0$ and a launch price can be agreed within this range, launch occurs. If not, negotiations may continue and launch may ultimately occur if either P_{sj}^{Offer} increases, P_{sj}^{Ask} falls, or some mechanism is negotiated to bridge the difference, such as a price-volume offset.[20]

[20] For example, France applies spending limits that result in price cuts if volume sold exceeds target levels.

In our data, we observe only the launch date and launch price conditional on launch, not the dates of registration approval or negotiation details. We therefore estimate reduced form equations for the launch hazard and launch price as a function of the determinants of the firm's ask price and the regulator's offer price. The reduced form launch hazard equation is:

$$h_{sjt} = h\{P_{bjt-1}, P_{gjt-1}, Q_{jt-1}, X_{jt-1}, N_{bjt-1}, N_{gjt-1}, I_{jt-1}, Y_j; P_{sKt-1}; H\} \quad (2)$$

Measurement and predicted signs of variables are discussed below.

Because the bargaining range $P^{Offer} - P^{Ask} > 0$ also defines the range of launch price, the reduced form launch price equation includes the same variables as the launch hazard equation:

$$P_{sj} = f\{P_{bj}, P_{gj}, Q_j, X_j, I_j, Y_j; P_{sKt-1}; H\} \quad (3)$$

In theory, expected price and market size at global launch t_0 influence the decision to seek registration and hence the launch hazard, and hence could identify the launch hazard equation, whereas launch price depends on competitor price values only at launch. In practice, both pre-launch values and change over time of the expected price and quantity variables were insignificant in the launch equation, after controlling for contemporaneous values. Identification in the two-stage selection models therefore relies mainly on functional form, as discussed below.

We estimate separate models for new drugs launching in superior vs. inferior subclasses. Coefficient differences between these equations are expected due to dynamic competition and related factors. For example, a drug that is a late entrant in an old subclass with declining sales may not be worth launching unless it offers significant advantages over established products in the subclass or expects favorable treatment by local regulators or markets.

V. Data and Methods

Data

We use data from IMS Health's Midas database on drugs in 15 countries for 12 therapeutic classes, all of which experienced the launch of a new subclass shortly before or during our study period, 1992-2003.[21] The data for each molecule include active ingredient, originator corporation(s) and marketing companies, pack description, launch date, therapeutic class, and quarterly data on outpatient sales at manufacturer prices (revenue in local currency) and unit volume (IMS standard units)[22] from 1Q 1992 through 4Q 2003. After the data were screened for internal consistency, revenue was adjusted for inflation using country-quarter-specific Producer Price Indexes available from the International Monetary Fund, with 2003 as the base year, and converted to US dollars using the average 2003 country-specific exchange rate. Price per dose for each drug was calculated on a quarterly basis as the ratio of total revenues to standard units sold.[23]

Of the 375 molecules in the dataset, 116 are classified as superior and 221 of their potential 1,740 drug-country launches had occurred prior to our study period; 259 are classified as inferior and 1,276 of their potential 3,885 drug-country launches had occurred prior to our period.[24] During our 12-year study period, we observe 885 of the 1,519 potential superior drug-

[21] Our 15 countries include all 5 large EU markets (UK, Germany, France, Spain and Italy) and both high and low price smaller EU countries (Sweden, Netherlands, Portugal and Greece). Omitting the other 6 small EU countries (Austria, Belgium, Denmark, Finland, Ireland and Luxembourg) would lead to biased estimates only if they were systematically different from the included countries. Country-specific spillover effects depend on the relative size and prices of referring and referenced countries (see eq. 1).

[22] The IMS standard unit is a proxy for a dose for each formulation e.g. one tablet or capsule, 5ml. for liquids. The IMS price data for the US do not reflect off-invoice discounts given by manufacturers to health plans and hence are upward biased for manufacturer net revenues.

[23] We combined multiple form-3 level formulations (e.g. tablets and capsules, possibly of different strength) in a given country and quarter into a single observation and defined the price as the volume-weighted average price per unit. Identical forms that were launched by different co-marketing companies were also averaged.

[24] Classification of molecules as superior or inferior was based mainly on mechanism of action, with input from several physicians and review of articles in PubMed (see Berndt, Danzon and Kruse, 2007). Our analysis includes only the first launch of each compound. We exclude follow-on indications or formulations because they typically face fewer registration requirements and pricing would be based on the price of existing formulations. We also focus on launch by an originator or licensee corporation, excluding the few cases of prior launch by copycat products. Five superior molecules and 20 inferior molecules were diffused to all our countries prior to our period. These are included as competitor products but are not in the sample of potential launches.

country launches and 390 of the 2,609 potential inferior drug-country launches. We observe 1,367 country-molecule-product launches (946 superior and 421 inferior) in our study period.[25]

Launch Estimation

We estimate the launch hazard using a maximum likelihood discrete time implementation of a proportional hazards model based on complementary log-log regression.[26] In the clog-log analysis, each drug was eligible for launch in all countries starting from its quarter of first launch in any country in our sample ("global launch"), and remained eligible until it launched. Thus each drug *s* in each country *j* contributes t_{sj} observations, the number of quarters from product *s*'s global launch through either first launch in country *j* or 4Q 2003, the end of our study period.[27] To account for the intra-molecule clustering across countries, we used robust standard errors or molecule random effects.

The hazard of launch is h_{sjt}, the probability that drug *s* launches in country *j* in period *t* conditional on not having previously launched. Using a clog-log specification implies that

$$h_{sjt} = 1 - \exp\left\{-\exp\left(\lambda(t) + \beta\Gamma_{sjt}\right)\right\} \quad (4)$$

where Γ_{sjt} is a vector of explanatory variables as outlined above. To facilitate interpretation, we present marginal effects calculated at the regressors' mean values. The standard errors of the marginal effects were calculated using the delta method; see Bartus (2005) for more details.[28]

One potential limitation of this specification is the assumption that the probability of launch goes to unity as time goes to infinity. Some of the molecules in our sample might not

[25] For 91 country-molecule pairs, two distinct formulations (form 2-level, such as an oral solid and a liquid) of a molecule launched simultaneously, and in four country-molecule pairs three distinct formulations launched simultaneously.

[26] Clog-log is preferred to logit because the former assumes a continuous launch decision process (Allison, 1995).

[27] Thus, although the first-stage results report thousands more observations than the second-stage results, the number of drug-country launches is the same in the first and second stages.

[28] We calculated marginal effects for interactions of dummy variables X_1 and X_2 as $\{[F(X\beta|X_1=1,X_2=1) - F(X\beta|X_1=0,X_2=1)] - [F(X\beta|X_1=1,X_2=0) - F(X\beta|X_1=0,X_2=0)]\}$, where F is the inverse of the clog-log function, $1 - \exp[-\exp(X\beta)]$. Other regressors were held at their means or at zero if they were related to X_1 or X_2. Standard errors were calculated using the delta method.

meet drug approval requirements or would have limited market potential in some countries. We therefore also estimate a discrete-time split-population model with time-varying covariates (Schmidt and Witte, 1989; Jenkins, 1995), which allows for some empirically-estimated sample-wide proportion of drugs never to launch.[29]

A second limitation of the clog-log specification is failure to account for possible time-invariant unobserved characteristics common to a molecule across countries that influence launch. Unobserved heterogeneity may lead to coefficient attenuation and biased estimates of duration dependence (Heckman and Singer, 1984; Lancaster, 1990). We address this issue by adding a Normally-distributed term for the drug-level heterogeneity ν_s:

$$h_{sjt} = 1 - \exp\left\{-\exp\left(\lambda(t) + \beta\Gamma_{sjt} + \nu_s\right)\right\} \quad (5)$$

Launch Price

We use ordinary least squares with molecule-clustered standard errors to model the log of launch price of drug *s* in country *j*, conditional on launching. To account for unobserved molecule characteristics we also report results from a GLS random effects estimator. To account for possible selection bias produced by the correlation between the propensity to launch and the launch price, we also estimate a Heckman selection model with a first-stage clog-log regression, which, as described above, is equivalent to a proportional hazards model of new drug launch.[30]

Variable Definitions

[29] This feature is especially relevant for analysis of molecules in inferior subclasses, in which 116 of the 259 molecules did not experience a new launch during the study period (compared with two of the 116 molecules in superior subclasses).

[30] The clog-log-based Heckman model is estimated following a two-step procedure that ensures consistent standard errors (Heckman, 1979). Following Lee (1983) and Greene (1992), the inverse Mills' ratio for drug *s* in country *j* and time *t*, M_{sjt}, is calculated using the predicted probability of launch $\hat{p}_{sjt}$ from a clog-log regression as

$$M_{sjt} = \frac{\phi\left[\Phi^{-1}\left(\hat{p}_{sjt}\right)\right]}{\Phi\left[\hat{p}_{sjt}\right]}$$

where $\phi[\cdot]$ is the standard Normal density function and $\Phi[\cdot]$ is the standard Normal distribution function. We also estimated a FIML Heckman model based on first stage probit that offers robust, clustered standard errors.

Regulation/Expected Price: We use the (log lagged) unweighted average price of competitor brand (originator and licensed, including parallel imports) products in the same therapeutic class as a comprehensive measure of the direct effect of price regulation on expected price for a new drug. The price of one or more competitor products is the explicit regulatory benchmark in internal referencing regimes; it should also be a rough proxy for the net effect of external referencing formulae. In free-pricing countries, the average price of established products provides an estimate of the expected price of a new drug, assuming competition constrains similar products to have similar prices. Average prices for superior and inferior subclasses are distinguished, to test for differential effects within vs. between subclasses, as proxies for static vs. dynamic price competition in free pricing countries; in regulated markets, analogous effects operate via the regulator's choice of comparator products.

Expected Sales Volume: The (log lagged) total number of doses sold in the same therapeutic class as the new drug is included as a measure of expected volume.[31] The expected effect on launch hazard and price is uncertain *a priori*, depending on whether the firm's opportunity cost of delay dominates the regulator's concern over budget impact. It was insignificant and was dropped from the price equation to conserve degrees of freedom.

Spillovers: To test for indirect effects in low-price countries of regulatory referencing by high-price countries, we included three count variables that measure the number of countries a molecule has already launched in, categorized by low-price EU countries (France, Italy, Spain, Portugal, Greece), high-price EU countries (Germany, the Netherlands, Sweden and the UK) and high-priced non-EU countries (the US, Japan and Canada). Our categorization of low- and high-price EU countries is supported by actual average prices (see below). These variables are also interacted with indicators for whether the potential launch is in a low- vs. high-price EU country.

[31] Measures of volume by subclass and number of competitors were not significant and were dropped.

These interactions test whether spillover effects are greater for launches in low-price EU countries, which are referenced by and are the main sources of parallel trade to higher-price EU countries, and whether spillovers are greater within the EU than from non-EU to EU countries, as expected.

In the price equation, we include similar interactions, except that we use the Minimum Own Price in high-price EU, low-price EU and high-price non-EU countries, defined as the lowest price received for the molecule in any country where launch has already occurred, for each country group, rather than simple count variables for number of prior launches. Estimates using Maximum Own Price were similar to those reported here using Minimum Own Price. Both variables could not be included together due to collinearity.[32]

We also include a dummy variable Any PI Share in Subclass, to test whether risk of competition from parallel import reduces the propensity to launch or reduces launch prices.[33] Because the IMS data do not identify the country from which PIs originate, we cannot test directly whether volume of parallel exports reduces launch hazards in exporting countries. Rather, the propensity to parallel export is subsumed in the country fixed effects.

First Mover Advantage and Timing: To test for first mover effects, the launch equation includes an indicator variable for quarters in which there are no molecules in the country-subclass. The price equation includes indicator variables for whether a launch was the first, second or third entrant in country-subclass.[34]

A quadratic in years since global launch is included to control for the decline in incentives for launch with time lapsed since global launch, because patents run regardless of

[32] We estimated specifications of the launch and price models that measured spillovers with either the number of countries previously launched in or minimum/maximum own prices. The specifications reported here yielded the better model fit and conceptual fit with the dependent variables.
[33] We estimated a model specification that included the average price of parallel imports, and it was not significant.
[34] The first mover advantage variables are based on the number of branded competitors by subclass, N_{bjt}.

launch and compounds may undergo obsolescence due to entry of newer compounds. An indicator for molecules launched before 1990 controls for their relatively old age. An indicator for molecules launched since 1996 tests for effects of the EMEA regime. It is expected to be positive if the cost-reducing effects of the EMEA coordinated registration process outweighed the increased risk of spillovers. Molecules launched during 1990-1995 are the referent category.

Country of Domicile: Previous studies have found that new drugs launch more quickly in the home country of the originator firm (Danzon, Wang and Wang, 2005; Kyle, 2006, 2007); however, differences across countries, by type of local firm, and effects on launch prices have not been examined. We include dummy variables to test for differential effects of three categories of local corporations: Local Originator identifies a molecule's originator corporation launching in its country of domicile; Solo Licensee identifies a locally-domiciled, licensed corporation that launched the molecule in at least one country by itself; and Local Co-marketer identifies a locally-domiciled, licensee corporation that launched together with another firm in its home country and did not launch alone in any country. The Solo Licensees are firms that have demonstrated ability to obtain drug registration on their own; thus their local expertise should be positively associated with launch hazard, and possibly also with price. The Local Co-marketers have not demonstrated registration expertise, hence they are predicted to have less effect on launch hazard than for either Originator or Solo Licensee firms; however, Local Co-marketers may affect price. These categories are not mutually exclusive; for example, a molecule with a small Local Originator could also have a Solo Licensee or a Local Co-marketer as a marketing partner, all from the same country.

Country and Year Effects: We include country fixed effects to capture other country-specific factors that may affect launch delay and launch prices (controlling for expected price,

volume and per capita income), in particular, pure bureaucratic delay and parallel export risk. Germany is excluded as the referent country.

The dollar-euro/ECU exchange rate and the PPI are included in the price equation to control for exchange rate and indexing trends that could bias our dollar-denominated estimates of competitor prices and launch prices. Year effects were included in some specifications, but were generally insignificant and are not reported here.

Product Characteristics: The price equation includes product characteristics that affect price per dose, including pack size, pill strength (grams per unit), and indicator variables for specialized formulations (oral delayed and non-oral solids), with oral solids (basic tablets and capsules) as the referent formulation.

VI. Descriptives

There are substantial differences in the number and timing of molecule launches by country and subclass (Table 1). For the superior subclasses, Germany and the US (two free pricing countries) have the most molecules ever launched (88 and 86). Sweden, the US, the Netherlands, Germany, and the UK (all higher price, less-strictly regulated) also have the shortest median launch delay (17.4-18.7 months). Japan, Portugal and France (all strict price-regulated countries) have the fewest superior molecules (53, 62 and 69 respectively) and the longest mean launch lags (41, 31, and 37).

For the inferior subclasses, Japan leads in number of inferior molecules (158) ever launched, followed by Germany (131), and even Portugal (113) has more than the US (97). The number of inferior molecule launches during our period is highest in three regulated markets (Japan [43], Brazil [40] and Greece [47]) whereas most other countries have fewer than 27.

Mean launch lags are generally much longer for inferior than for superior molecules. These differences in launch experience in the superior vs. inferior subclasses confirms that the older subclasses may be more heterogeneous, including some molecules that could not meet strict regulatory requirements and/or have limited sales potential in some markets.

Table 2 reports the mean number of manufacturers per molecule in 2003 by country, subclass and license type, to illustrate differences in market structure. The expected number of originator/licensee firms per molecule is 1-2, assuming that an originator's profit-maximizing strategy is usually to launch alone or with at most one co-marketing partner. Consistent with this, the mean number of originator/licensee firms per superior molecule is 1.0 in the US, the UK, and the Netherlands, and only slightly higher in most other countries. Licensees are more common in Italy (1.8), Spain (1.7) and Japan (1.3), suggesting that having a local co-marketing partner may be particularly valuable in these countries. Parallel imports are found only in the four higher priced EU countries—Germany, the Netherlands, Sweden and the UK—and the majority of molecules in these countries have some PI presence by 2003. This concentration of PIs in a few countries may provide insufficient variation to estimate PI effects accurately, as noted below.

Table 3 reports unweighted mean prices by country-subclass-license type, to provide a rough measure of benchmark competitor prices used by regulators and firms in forming price expectations. Note that these means reflect differences in molecules and formulations, in addition to price differences for identical products, and hence are not valid indexes of cross-national price differences for a standardized basket of drugs.[35]

These unweighted mean prices show that, for originator/licensee superior products in the EU, the strictly price-regulated regimes (France, Spain, Portugal, Greece, Italy) have relative low

[35] Danzon and Furukawa (2003, 2008) report weighted price indexes, based on standardized market baskets, for originator and generic products in 1999 and 2005

prices. Thus, we classify them as "low-price EU markets." The countries with freer pricing, reimbursement regulation and/or late adoption of price regulation (Germany, the UK, the Netherlands, Sweden) have higher mean prices, and we classify them as "high-price EU markets." The US has the highest prices, followed closely by Canada; we also classify Switzerland and Japan as "non-EU high-price markets" based on other price index comparisons (Danzon and Furukawa, 2003), although Japan's unweighted mean prices are quite low in Table 3. Originator prices are lower in inferior than superior subclasses, and country rankings are similar but with smaller differentials. Other Brand prices are generally higher than for Unbranded Generics, as expected.[36] PI prices generally fall between generic and originator prices, as expected; however, these differentials are not based on a standardized product mix and do not provide an accurate measure of originator/PI price differentials.

Table 4 shows, for each country, the number of molecules launched by a Local Originator, a Solo Licensee or a Local Co-marketer corporation, and the average number of countries in which each country's originated molecules were launched. Using launch by a Local Originator as a proxy to identify molecules originated in each country, for superior drugs, the US originated the largest number (30), followed by Japan (17), and the UK, France and Switzerland (11 each). All other countries had 0 to 4 launches. Drugs originating in Japan and Spain diffused to dramatically fewer countries on average (4) than drugs originating in other countries (10.6-12.8). Japan originated the largest number of inferior molecules (45), compared to the US (29), Germany and Switzerland (25-26). All countries other than the US originated more inferior molecules than superior molecules. In general, inferior molecules diffuse to fewer countries than superior molecules.

[36] Some of the PI, Unbranded Generic and Other Brand means include very few products. For unbranded generics, the relatively high mean US price is surprising and reflects its product mix, whereas volume-weighted price indexes for standardized products show low generic prices in the US (Danzon and Furukawa, 2003).

Means and standard deviations for variables in the launch and price equations are reported in Appendix Tables A1 and A2.

VII. Determinants of Launch

Table 5 reports coefficients and marginal effects from our basic launch specification, using clog-log estimates with either robust, clustered standard errors or molecule-level Normal random effects to control for unobserved molecule characteristics.[37] Country and class fixed effects are included. Our discussion focuses on estimates for the superior subclasses, noting differences for the inferior subclasses where relevant.

Direct Effect of Price Regulation

Launch hazards are significantly related to mean prices of competitor brands in the same subclass: for superior products a 10 percent increase in competitor prices is associated with a 0.054 percentage point increase in the launch hazard, which implies an elasticity of 0.14 at the 3.8% mean launch hazard for superiors molecules per quarter. Thus to the extent that regulation reduces prices, it reduces incentives to launch. These estimates may underestimate the magnitude of regulatory effects, if our measure of mean price, based on all originator and licensed products in the subclass, includes some that are not used as comparators by regulators. For the inferior subclass, the own subclass price effect is positive but only marginally significant. Cross-class price effects are insignificant, indicating that regulatory benchmarking and/or competitive constraints operate primarily within rather than between subclasses, and that dynamic competition is driven by product characteristics other than price. Similarly, the effects of number of generic competitors are negative but statistically insignificant, providing further evidence that availability of older, cheaper generic substitutes is not a significant deterrent to the

[37] Parallel specifications using a split population clog-log model were generally consistent with those reported here.

launch of new brand products, even in older subclasses where generics are more numerous, possibly because generic substitution is mostly within rather than between molecules.

Unit volume for the therapeutic class—whether measured contemporaneously, at global launch, as a growth rate or by subclass—was not significant. This may reflect offsetting incentives for regulators to constrain prices more stringently for compounds with large potential sales, whereas firms prefer to launch these drugs more promptly.[38]

Launch Timing and Sequence

For both superior and inferior products, launch hazards appear first to decrease then increase with time since global launch, reaching a minimum at 13.5 yrs from global launch for superior drugs and 49.0 years for inferiors.[39] These average quadratic specifications reflect the diverse launch patterns in Table 1, which shows median launch lags for superior drugs of less than one year in the high-price EU countries and the US, followed by launch within the second year for all other countries except France, Portugal and Japan, where launch typically occurs later. For inferior drugs, median launch lags are much longer.

Inferior drugs launched before 1990 are more likely to launch than later entrants in the same subclass, possibly due to accumulated global brand capital of these earlier entrants and despite their presumably shorter remaining patent life.[40] The poor launch performance of late entrants in older subclasses further confirms that dynamic competition from newer subclasses disadvantages late entrants to older subclasses.

[38] The insignificant effects of volume on launch of new products found here contrasts with significant positive effects in Danzon, Wang and Wang (2005). These different findings may reflect differences in sample countries and drugs, in addition to our use here of more detailed measures of country-class prices and other characteristics.
[39] The minimums from the split population estimates are 10.9 years for superior and 50.3 years for inferiors.
[40] Patent expiry is less critical to expected sales in countries with few generics or primarily branded generics that do not compete aggressively on price. This includes all the low-price EU countries during our time period.

The coefficient on the post-1996 global launch indicator is negative but insignificant for superior drugs. Taken at face value this suggests that on average the EMEA process has not reduced launch lags, possibly because price approval is the rate-limiting regulatory hurdle and any cost-reducing effect of accelerated approval is offset by increased risk of spillovers. Such inferences are tentative, however, because our analysis period is too early to observe the full effects of the EMEA, which focused initially on biologics and truly innovative drugs.

Indirect Regulatory Effects: Cross-National Spillovers

The evidence strongly supports the hypothesis that launch in low-priced EU countries is adversely affected by the risk of spillover to higher-price EU countries through external referencing and possibly PI risk. For superior drugs, the coefficients on number of countries in which launch has already occurred are positive and significant, with the exception of prior launch in the three lowest price EU countries, Spain, Portugal and Greece. The marginal effect is largest for prior launch in the UK or Germany, at 0.030, and is 0.025 for prior launch in Sweden or the Netherlands. By contrast the marginal effect of prior launch in Italy or France is 0.013, and for high price non-EU countries the marginal effect is only 0.009.[41] This pattern confirms that firms delay launch in low-price EU countries until launch has occurred in higher-price EU countries. Moreover, because Spain, Portugal and Greece reference the lowest prices in a group of relatively low-price countries, including France and Italy, a firm's optimal launch strategy plausibly leads to launching last in these three countries, after higher prices have been established in the countries that they reference. For inferior drugs, marginal effects are much smaller and generally insignificant, consistent with other evidence that these late launching drugs in older subclasses have atypical launch potential.

[41] The p-values for Wald tests comparing these marginal effects are as follows: UK/Germany vs. Italy/France, p=0.019; UK/Germany vs. high-price non-EU countries, p=0.009; Sweden/Netherlands vs. Italy/France, p=0.062; Sweden/Netherlands vs. high-price non-EU countries, p=0.003.

To explore further the spillover effects for superior drugs, we estimated a specification that includes counts of prior launches in high-price EU, low-price EU and other high-price countries (Canada, Japan, Switzerland and the US), together with interactions between these launch counts and indicators for whether the current observation is a low- or a high-price EU country. Marginal effects of these interactions are reported in Table 6. The marginal effect of a prior launch (from zero to one) in a high-price EU country on launch in a low-price EU country is 0.0018, whereas the effect of a prior launch in another low-price EU country is only 0.0005, and the difference is statistically significant. Similarly, the marginal effect on launch in a low-price EU country is greater from a prior launch in a high-price EU country than from a launch in a high-price non-EU country, as expected, because referencing and parallel trade within the EU is only to EU countries. This evidence is thus consistent with the hypothesis that the observed pattern reflects spillovers, not simply some unobserved factor that leads to correlation in launch timing across countries.

Parallel import presence in the class is not associated with launch hazard in the importing country, after controlling for country fixed effects. This may simply reflect the high correlation between the PI indicator and the country indicators for the four importing countries—Germany, Sweden, the Netherlands and the UK—and the high PIs presence across classes in those countries. It is also more likely that parallel trade risk leads primarily to non-launch or launch delay in the parallel export countries, not in the importing countries. We cannot measure this effect in the exporting countries because our data do not report PI country of origin; hence it is subsumed in country effects.[42]

Launch by a Local Corporation

[42] We tried including the average price of PIs, but this was not significant.

Launch is more likely for both superior and inferior molecules from firms that are domiciled domestically. For superior drugs, the marginal effect of launch by a Local Originator is 0.13-0.18, compared with 0.03-0.04 for Solo Licensees and 0.02-0.03 for Local Co-marketers. This ranking confirms that compounds that are originated by local firms have significantly greater local advantage than compounds that are simply represented by local licensee firms,[43] although even the latter accelerate launch somewhat relative to having no local connection. Firms that are local originators by definition have local R&D activities and hence are likely to be larger, have greater regulatory expertise and be viewed as more valuable to the local economy than firms that are just co-marketers, with Solo Licensees in the middle. To test whether these local corporation effects differed across countries, we combined the three indicators into a single Any Local Corporation indicator and estimated a specification with interactions between Any Local Corporation and country fixed effects.[44] Marginal effects of these interactions are reported in Table 7. The effect of the Any Local Corporation indicator is insignificant for the referent, Germany, and for most other countries. The exceptions are France, Italy, Spain, Switzerland and Japan, where launch by a local corporation has a significant positive effect for superior drugs. Overall, this evidence indicates that the large positive mean local corporation effect on launch hazard, observed in our baseline specifications and in previous studies, is confined to a few countries, with no significant domestic advantage in most countries. This suggests that the local corporation advantage reflects primarily industrial policy to support local firms in certain countries, not that local firms in general have greater expertise in dealing with local regulatory systems in all countries.

[43] $P < 0.05$ for comparisons of marginal effects between Local Originators and either Solo Licensees or Local Co-marketers.

[44] We tried to estimate a specification with interactions between each of the three local corporation indicators and country fixed effects. The clog-log coefficients could not be estimated due to small sample sizes for several countries.

To shed further light on cross-national differences, Appendix Table 3 reports the number of launches and mean and median launch lags for launches by Local Originators, Solo Licensees and Local Co-Marketers compared with launches by non-local corporations, by country. For Japan, the mean launch delay for superior drugs is 1.8 months with a Local Originator, compared with 53.0 months with no local firm, and 59 months with a Solo Licensee and 49 months with a Local Co-marketer. The Local Originator advantage could partially reflect the fact that clinical trials for these drugs were probably done on Japanese subjects, as required for registration in Japan. However, the fact that these Japan-originated drugs on average diffused to only 4 countries besides Japan indicates that their home advantage is not just speed due to local trials; rather, it reflects a tendency for Japan to approve locally-originated drugs that have limited potential in other countries. In France, Italy and Spain, there is some evidence that launch lags are shorter if a Local Co-marketer is present than if the drug is launched by a Solo Licensee. This is consistent with the hypothesis that Local Co-marketers are added only where they are expected to bring advantage to foreign originators in dealing with regulators; it is also consistent with anecdotal evidence that regulators in these countries traditionally encouraged such co-marketing as industrial policy to support local firms.

Country Fixed Effects

For superior drugs, compared to Germany, the referent country, other country effects are all negative. Marginal effects are smallest for the UK (-0.011) and other relatively free pricing countries; marginal effects are largest for Japan (-0.044), reflecting its unique registration requirements; and the major EU parallel export countries (Spain, France, Greece, Portugal and Italy) are all significantly negative, as are several other countries. For inferior drugs, none of the country marginal effects is significant in the basic clog-log estimation, possibly due to within-

class heterogeneity. However, for the US, the clog-log coefficient, the RE marginal effect and the split population estimates are all negative, implying that late-launching inferior drugs are less likely to launch in the US than in other countries.

Split Population and Random Effects Estimators

The split population and random effects estimates are generally consistent with the clog-log estimates. However, the split population estimates (available from the authors) imply that the probability of never launching is highly significant for 27.7 percent of inferior molecule-country pairs, compared with only 4.9 percent of the superior molecules. This provides further evidence that certain molecules, especially late entrants in inferior classes, are not marketable in certain countries.[45] Whether this reflects inability to meet regulatory or market requirements cannot be determined with our data.

VIII. Determinants of Launch Price

Table 8 reports the determinants of (log) launch price using OLS with robust, clustered standard errors, and GLS random effects to control for unobserved molecule heterogeneity. Our discussion focuses on estimates that include GDP per capita; excluding GDP changes primarily the country fixed effects, as reported below.[46] Year fixed effects were also included, to control for any bias in our inflation and exchange rate adjusters, but these coefficients were generally

[45] The estimated percent never launching is significantly higher once we control for Local Originator Corporation, suggesting that some countries approve locally-originated drugs that have limited diffusion potential elsewhere.

[46] Because our observed launch prices are conditional on launch, we estimated both a two-stage Heckman selection correction model that includes as a regressor the inverse Mills' ratio from a clog-log first-stage hazard equation and a traditional FIML Heckman model based on a probit first-stage equation. The coefficients on the inverse Mills' ratios are larger for the inferior drugs, but are significant only for the superior drugs (and only in the two-stage models); otherwise results are generally similar to the conditional estimates. These results are broadly consistent with the finding from the split population estimates that at least some molecules do not have global launch potential. Because the first-stage launch equation is identified primarily off functional form, we focus our discussion on the conditional estimates in Table 8 and do not attempt to draw inferences about differences between conditional and unconditional estimates.

insignificant and are not reported. Therapeutic class effects were omitted because they are highly collinear with competitor prices and order of entry within class.

Competitor Prices

For both superior and inferior products, launch prices are significantly positively related to prices of competitor products in the same subclass (elasticity of 0.12 for superiors and 0.17 for inferiors). The cross-subclass elasticity of inferior drug prices on launch price of new superior drugs is also positive but smaller (0.08). This confirms the earlier evidence, that launch hazards are influenced mainly by prices of established products within subclass, implying that dynamic competition between subclasses is based on non-price product attributes. Generic prices have no significant effect on launch prices of new superior brands, suggesting weak price competition between new brands and old generics. Launch prices of new inferior products are affected negatively by generic prices in the class (elasticity -0.09), which may reflect a selection effect: late entrants in inferior subclasses launch only if they expect to receive high prices relative to competing generics.

Launch Timing and Sequence

Controlling for inflation and exchange rates, launch prices for superior products decline with time elapsed since global launch, at an estimated rate (from the random effects model) of -3.8% (p=0.05) per year.[47] This suggests that manufacturers cannot obtain a higher price simply by holding out.

For superior products, there is no evidence of first-mover advantage in prices, although second and third entrants do receive higher prices relative to later entrants in a class. For inferior products, the first or second entrants in the subclass appear to receive a price premium relative to

[47] The net impact of time since global launch (a quadratic) was calculated as $\beta_{tsgl} + 2\beta_{tsgl^2}\bar{t}$, where the mean value of time is 2.16 years.

other inferior drugs. This conclusion is tentative, however, because it is based on a very small number of inferior subclasses for which first and second launches occur in our time period.

Cross-national Spillovers

For both superior and inferior products, launch prices increase with the lowest price previously received in other high-price EU countries, whereas effects of launch in low-price EU countries is insignificant. The minimum own price received in non-EU countries is significantly positive for superior molecules, but insignificant for inferior molecules, which launch less frequently in high-price non-EU countries such as the US and Canada.

We also estimated equations with interactions to test the hypothesis that spillovers to low-price EU countries are largest from high-price EU countries. Marginal effects of the interactions are reported in Table 9, which parallels Table 6 for the launch model in structure and results. We find that the effect on launch price in a low-price EU country is larger for a 10% increase in a drug's minimum own price in high-price EU countries than from a 10% increase in minimum own price in other low-price EU countries. Specifically, the difference in the marginal effects in the minimum own price elasticity based on the OLS model is 0.39, and based on the RE model is 0.26. Similarly, the effect on launch price in a low-price EU country is substantially larger for a 10% increase in a drug's minimum own price in high-price EU countries than it is for a 10% increase in minimum own price in high-price non-EU countries. The differences in the own price elasticity are 0.37 from the OLS model and 0.24 for the RE model, consistent with the hypothesis that launching first in high-price EU markets can influence prices in low-price EU markets. This evidence from launch prices thus validates that launch delay in low-price markets may ultimately yield higher prices in these markets through spillovers from higher-price markets, in addition to avoiding contamination of those high-price markets.

The indicator for PI presence is insignificant for superior drugs, but significant and negative for inferior drugs, indicating that PI presence reduces launch prices mainly for late entrants in older subclasses.

Local Corporations

For superior drugs, launch by a Local Originator is positively associated with launch price, but the effect is not significant. Estimated effects of both types of licensees are negative but insignificant. For inferior drugs, the average effect of launch by a Local Originator is significantly negative, which may reflect the fact that these late-launching inferior drugs have relatively weak characteristics, relative to established drugs in the subclass. The fact that the RE effects are smaller than the OLS effects is consistent with this. Launch by a Local Licensee is negative but insignificant. Tests for country-specific differences in local corporation effects (results not shown) are generally insignificant. This lack of evidence of a price premium for drugs launched by local firms, despite a significant advantage in the launch equation for a subset of countries, suggests that the launch advantage reflects favoring by the registration authorities rather than by pricing authorities. However, conclusions are tentative due to small sample sizes.

Macroeconomic Controls

The US dollar per euro/ECU exchange rate, which declined from a high of 1.38 in 1992 to a low of 0.83 in 2000, is insignificant for superior products but large and significant for inferior products. This suggests that our exchange rate adjustments accurately tracked manufacturers pricing adjustments for the more broadly diffused superior products, which are at higher risk of referencing and parallel trade. By contrast, our exchange rate adjustment apparently over-adjusted for launch pricing for inferior products, which were less likely to launch in the US and therefore plausibly, were priced independently of the USD/Euro exchange

rate.[48] For superior drugs, the country-specific Producer Price Index (our price deflator) is significantly negative in the OLS specification, suggesting that launch prices of drugs on average have not kept pace with economy-wide inflation, but this conclusion is tentative because the RE estimate is insignificant.

Product Characteristics

Product characteristics have expected effects. Price per unit is significantly negatively related to pack size, particularly for pack size over 100 units, possibly indicating economies of scale in packaging and/or the competitive use of large packs to give discounts to pharmacies in countries such as the US, that permit pharmacists to dispense from large packs. Price is unrelated to strength (grams of active ingredient per unit) in the RE estimates, suggesting that the positive coefficient in the OLS results for superiors reflects between- rather than within-molecule effects. Compared to the oral solid formulations (the omitted category), price per dose is significantly higher for injectable and non-oral forms (liquids, creams etc).

Country Fixed Effects

The country fixed effects in Table 8 are dramatically different depending on whether GDP per capita is included. Based on the RE estimates, without GDP controls, prices for superior molecules in the US and Japan are significantly higher than in Germany; prices in Switzerland and Canada are higher but insignificant, whereas prices in Brazil, Mexico and all other EU countries are lower, except the Netherlands and Sweden which are similar to Germany. However, after controlling for GDP per capita, Brazil, Mexico, Spain, Portugal and Greece have prices significantly higher, and Switzerland, the UK and Sweden have prices significantly lower than Germany.

[48] If manufacturers priced inferior drugs based on local prices that were flat or falling in ECUs, the prices would be rising over time in USD, due to USD devaluation, thus explaining the positive and significant coefficient on the exchange rate variable.

Although these are not pure hedonic country effects, taken at face value they imply that the prevailing spread in drug prices across EU countries is compressed relative to the counterfactual of differentials based on per capita income. This may explain at least in part why Spain, Portugal and Greece, the lowest-price EU countries in our sample, adopt more stringent price controls than the higher-price northern countries. However, these low-price EU countries appear to be constrained in their ability to keep price differentials in line with income differentials, in part due to external referencing by and parallel importing to higher-income countries. The evidence here confirms that the resulting interconnectedness across countries contributes to delay or non-launch of new drugs in these low-price EU countries, as firms seek to avoid spillovers to prices in higher-price EU countries.

IX. Conclusions

Our findings demonstrate that launch timing and launch prices of new drugs are significantly related to prices of established products in the same subclass. Thus, to the extent price regulation reduces price levels, it contributes directly to the longer average launch delays observed in low-price countries. Our estimates suggest that the magnitude of these direct effects is quite small, although downward bias due to measurement error is possible. Welfare conclusions are ambiguous, assuming that regulators weigh the benefits of lower prices against any welfare loss from reduced access to new drugs for their citizens.

We also find significant evidence that regulatory referencing by high-price countries to lower-price countries within the EU creates incentives for manufacturers to delay launch in low-price countries until higher prices have been established in other countries. Consistent with such strategies, launch in higher-price EU countries is associated with increased launch hazard in

lower-price EU countries, and launch prices in low-price EU countries are directly related to prior launch prices in high-price EU markets. This evidence, that spillover effects are greater from high-price EU countries to low-price EU countries, than from high-price non-EU countries, in both launch and price models, supports the hypothesis that they are attributable to referencing and possibly parallel trade, not to other unmeasured factors that may lead to closely sequenced launches across countries. To the extent that referencing or parallel importation by higher-price countries leads to longer launch delay or higher prices in lower-price countries than would otherwise occur, a welfare loss is imposed on low-priced countries by the higher-price countries that adopt these regulatory strategies. We find no evidence of first mover pricing advantage, and no evidence that manufacturers can raise prices simply by delaying launch.

Although the lower-income EU countries regulate their drug prices, Spain, Portugal and Greece nevertheless had relatively high drug prices given their income, whereas high-price EU countries had lower drug prices relative to their per capita GDP. Both the theory and evidence presented here suggest that external referencing has contributed to this convergence of pharmaceutical prices relative to GDP among EU countries. Parallel trade effects are expected to be smaller, and empirical estimation is limited because our data do not identify exported volumes. With that caveat, the evidence suggests that parallel import threat reduces launch prices of late-launching inferior products, and that country fixed effects are negative for countries that are significant parallel exporters.

Although prices of new drugs are constrained by prices of established drugs, due to either regulation or competition, such effects occur primarily within subclasses, with weaker constraints from older, cheaper drugs. Late entrants in older subclasses diffuse less broadly than new drugs in newer subclasses, and these late inferior launches are at lower prices, linked to the

lower prices in these older subclasses. This evidence suggests significant dynamic competition on non-price product attributes in pharmaceutical markets, even though price competition and regulatory referencing are mainly within subclasses.

The positive effects of launch by a local corporation found in previous studies are confined in our sample to a few countries—France, Italy, Spain, Switzerland and Japan—and appear to reflect primarily local registration advantage for drugs originated by local companies. We find weaker evidence of benefits from use of local licensees as co-marketing partners, particularly in France, Italy and Spain. The fact that these local corporation advantages are confined to specific countries suggests that they reflect industrial policy strategies favoring local firms in these countries, rather than a more general local firm advantage based on experience in dealing with local regulation.

This evidence, that policies of external referencing (and, with weaker evidence, parallel importing) impose an external cost on the referenced or exporting countries, is based on the EU, where such policies already exist. However, it has important implications for the US debate over drug price controls through external referencing and drug importation. The theory above indicates that the launch lag externality will be greater if referenced countries are small and low price, compared to a much larger, higher-price referencing or importing country. Because the US has both higher brand prices and much higher total volume than most potential reference or exporting countries, the impact on these countries if the US were to adopt referencing or importing would potentially be much larger than the EU effects documented here.

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Table 1. Launch and Molecule Count and Mean and Median Launch Delay by Country and Subclass

	Superior Subclasses				Inferior Subclasses			
Country	Molecules	Launches	Mean Launch Delay	Median Launch Delay	Molecules	Launches	Mean Launch Delay	Median Launch Delay
High-Price EU Countries								
Germany	88	72	18.5	9.5	131	18	30.4	17.5
UK	80	58	18.7	6.5	116	24	69.2	41.5
Netherlands	73	56	18.1	10	112	21	43.7	15
Sweden	77	62	17.4	7	82	19	49.9	18
Low-Price EU Countries								
France	69	53	30.9	29	105	19	87.6	59
Greece	72	55	30.1	22	107	37	116.8	54
Italy	76	61	24.8	21	127	26	74.7	48.5
Portugal	62	48	37.0	33.5	113	26	85.8	67
Spain	76	62	28.1	21	112	23	43.9	31
High-Price non-EU Countries								
Canada	73	62	25.6	16	98	22	91.9	66.5
Japan	53	42	41.0	40	158	43	63.3	28
Switzerland	78	63	23.9	18	111	21	55.5	47
USA	86	72	17.9	8	97	23	86.4	62
Low-Price non-EU Countries								
Brazil	71	60	31.2	20.5	92	40	107.1	90.5
Mexico	72	59	28.6	17	105	28	84.0	55

Note: Launch delays measured in months

Note: Sample includes all molecules present and new launches occurring in our data during 1992-2003

Note: Launch delays are calculated only for country launches that occurred during 1992-2003 (regardless of when the global launch occurred)

Table 2. Mean Number of Manufacturers per Molecule by Country, Subclass and License Type in 2003

	Superior Subclasses					Inferior Subclasses				
Country	Originator / Licensee	Unbranded Generic	Parallel Import	Other Brand	Molecules	Originator / Licensee	Unbranded Generic	Parallel Import	Other Brand	Molecules
High-Price EU Countries										
Germany	1.2	1.6	4.2	1.3	86	1.3	3.0	3.0	3.3	114
UK	1.0	0.3	0.1	0.0	79	1.1	1.0	0.3	1.1	103
Netherlands	1.0	0.0	5.5	0.0	68	1.1	0.0	6.1	0.1	97
Sweden	1.1	0.6	1.2	0.1	73	1.1	0.5	1.4	0.2	74
Low-Price EU Countries										
France	1.2	0.6	N/A	0.0	66	1.2	2.0	N/A	0.4	98
Greece	1.1	0.1	N/A	1.4	70	1.0	0.1	N/A	2.1	93
Italy	1.8	0.5	N/A	0.6	74	1.4	1.0	N/A	2.0	105
Portugal	1.3	1.1	N/A	1.1	61	1.1	0.4	N/A	0.8	101
Spain	1.7	2.2	N/A	1.1	73	1.4	0.9	N/A	1.3	100
High-Price non-EU Countries										
Canada	1.1	0.4	N/A	0.8	69	1.1	2.0	N/A	1.7	85
Japan	1.3	0.4	N/A	1.5	52	1.5	0.3	N/A	3.3	153
Switzerland	1.1	0.1	N/A	0.2	77	1.1	0.2	N/A	0.5	93
USA	1.0	1.4	N/A	0.0	85	1.2	7.0	N/A	0.3	91
Low-Price non-EU Countries										
Brazil	1.2	1.2	N/A	2.1	68	1.1	1.4	N/A	3.0	84
Mexico	1.1	0.3	N/A	0.9	70	1.1	0.7	N/A	1.9	90

Note: Sample includes all molecules present in IMS dataset in 2003

Table 3. Mean Price per Molecule by Country, Subclass and License Type in 2003

	Superior Subclasses				Inferior Subclasses			
Country	Originator / Licensee	Unbranded Generic	Parallel Import	Other Brand	Originator / Licensee	Unbranded Generic	Parallel Import	Other Brand
High-Price EU Countries								
Germany	30.31	0.49	9.23	0.94	2.56	0.32	0.33	0.75
UK	13.26	0.64	1.36	0.61	6.18	0.93	0.46	1.27
Netherlands	35.53	0.05	2.22	7.75	10.79	0.45	0.61	0.72
Sweden	24.41	0.34	1.79	0.45	13.08	0.26	0.42	0.98
Low-Price EU Countries								
France	6.52	0.41	N/A	0.89	0.28	0.39	N/A	0.75
Greece	12.84	1.11	N/A	0.56	6.26	0.45	N/A	0.80
Italy	2.24	0.41	N/A	0.77	0.30	0.31	N/A	0.61
Portugal	1.83	0.44	N/A	0.78	0.33	0.20	N/A	0.34
Spain	6.13	0.33	N/A	1.06	0.28	0.63	N/A	0.69
High-Price non-EU Countries								
Canada	49.30	0.57	N/A	0.60	1.03	0.93	N/A	0.57
Japan	12.27	0.44	N/A	0.73	2.62	1.26	N/A	0.59
Switzerland	34.64	0.81	N/A	0.76	5.81	0.37	N/A	1.43
USA	52.70	0.90	N/A	14.22	11.05	1.43	N/A	12.72
Low-Price non-EU Countries								
Brazil	2.34	0.39	N/A	0.95	4.21	0.21	N/A	0.35
Mexico	18.34	0.69	N/A	1.65	5.84	0.26	N/A	0.53

Note: All prices are ex manufacturer prices per standard unit in 2003 US Dollars
Note: Sample includes all molecules present in our dataset in 2003

Table 4. Number of Launches and Mean Number of Other Country Launches by Country, Subclass and Domestic Status of Corporations

	Molecules in Superior Subclasses					Molecules in Inferior Subclasses				
		Local Originator Corporations		Solo Licensees	Local Co-marketers		Local Originator Corporations		Solo Licensees	Local Co-marketers
Country	Total Launches	Launches	Mean # Other Country Launches	Launches	Launches	Total Launches	Launches	Mean # Other Country Launches	Launches	Launches
High-Price EU Countries										
Germany	88	4	12.8	10	3	131	26	7.7	22	4
UK	80	11	12.7	7	0	116	18	11.1	11	1
Netherlands	73	0	N/A	0	0	112	2	12.5	3	0
Sweden	77	3	13.3	1	0	82	0	N/A	3	0
Low-Price EU Countries										
France	69	11	10.5	5	3	105	19	7.3	16	2
Greece	72	0	N/A	0	0	107	0	N/A	2	0
Italy	76	1	0.0	13	14	127	11	5.0	25	13
Portugal	62	0	N/A	2	2	113	0	N/A	5	2
Spain	76	2	4.0	5	7	112	8	5.1	11	4
High-Price non-EU Countries										
Canada	73	0	N/A	3	0	98	1	1.0	10	0
Japan	53	17	4.0	6	11	158	45	1.9	36	24
Switzerland	78	11	10.6	4	0	111	25	11.2	10	0
USA	86	30	10.6	20	0	97	29	9.6	33	1
Low-Price non-EU Countries										
Brazil	71	0	N/A	2	0	92	3	0.7	4	1
Mexico	72	0	N/A	0	0	105	1	0.0	2	0

Note: Sample includes all molecules present and all country launches occurring in IMS dataset through 2003

Note: Molecules with multiple local corporations in a country were assigned to a single one in the order of Local Originator, Solo Licensee or Local Co-marketer

Table 5. Coefficients and Marginal Effects for Launch Model (Standard Errors in Brackets)

	Coefficients				Marginal Effects			
	Clog-log with Robust Clustered SEs		Clog-log with Normal REs		Clog-log with Robust Clustered SEs		Clog-log with Normal REs	
	Subclass				Subclass			
Variables	Superior	Inferior	Superior	Inferior	Superior	Inferior	Superior	Inferior
Log Avg Price of Superior Brands (Lag 1Q)	0.1138**	-0.1089	0.1442***	-0.1202*	0.0053*	-0.0001	0.0086***	-0.0003
	[0.0552]	[0.0683]	[0.0476]	[0.0616]	[0.0027]	[0.0001]	[0.0032]	[0.0002]
Log Avg Price of Inferior Brands (Lag 1Q)	0.0658	0.1247*	0.0894*	0.0928	0.0031	0.0001	0.0053*	0.0002
	[0.0612]	[0.0697]	[0.0506]	[0.0609]	[0.0029]	[0.0001]	[0.0031]	[0.0002]
Log Total Volume of All Drugs in Class (Lag 1Q)	-0.0738	0.0829	-0.0202	0.1386	-0.0034	0.0001	-0.0012	0.0004
	[0.0527]	[0.1058]	[0.0581]	[0.0889]	[0.0027]	[0.0001]	[0.0035]	[0.0002]
Num Generic Manufs per Molc in Superior Subclass (Lag 1Q)	-0.0040	0.0035	-0.0079	0.0103	-0.0002	0.0000	-0.0005	0.0000
	[0.0045]	[0.0081]	[0.0059]	[0.0083]	[0.0002]	[0.0000]	[0.0004]	[0.0000]
Num Generic Manufs per Molc in Inferior Subclass (Lag 1Q)	-0.0016	-0.0030	-0.0014	-0.0023	-0.0001	0.0000	-0.0001	0.0000
	[0.0021]	[0.0031]	[0.0017]	[0.0025]	[0.0001]	[0.0000]	[0.0001]	[0.0000]
No Molecules in Superior Subclass D.V.	0.2585	-0.2298	0.1416	-0.2018	0.0135	-0.0002	0.0089	-0.0005
	[0.1848]	[0.2583]	[0.1947]	[0.2353]	[0.0105]	[0.0002]	[0.0129]	[0.0006]
No Molecules in Inferior Subclass D.V.	-0.5880***	-0.3552	-0.5529	-0.3155	-0.0210***	-0.0002	-0.0264	-0.0007
	[0.2181]	[0.8341]	[0.4677]	[0.5482]	[0.0074]	[0.0005]	[0.0181]	[0.0011]
Time Since Global Launch (Yrs)	-0.6240***	-0.2767***	-0.4540***	-0.2772***	-0.0291***	-0.0002**	-0.0271***	-0.0007***
	[0.0578]	[0.0323]	[0.0536]	[0.0288]	[0.0046]	[0.0001]	[0.0049]	[0.0002]
Time Since Global Launch Squared (Yrs)	0.0231***	0.0028***	0.0158***	0.0029***	0.0011***	0.0000**	0.0009***	0.0000***
	[0.0027]	[0.0004]	[0.0030]	[0.0004]	[0.0002]	[0.0000]	[0.0002]	[0.0000]
First Global Launch Before 1990 D.V.	-0.0034	0.5749**	-0.2426	0.7042**	-0.0002	0.0006*	-0.0131	0.0023**
	[0.1931]	[0.2743]	[0.2860]	[0.3089]	[0.0090]	[0.0003]	[0.0149]	[0.0011]
First Global Launch in [1996-end] D.V.	-0.0497	-0.0329	-0.1018	-0.0383	-0.0023	0.0000	-0.0058	-0.0001
	[0.1479]	[0.2194]	[0.1907]	[0.3420]	[0.0066]	[0.0002]	[0.0108]	[0.0009]
Num Already Launched (UK, Germany)	0.5935***	0.5632***	0.4902***	0.4131***	0.0290***	0.0004	0.0301***	0.0011**
	[0.0920]	[0.1848]	[0.0785]	[0.1466]	[0.0071]	[0.0003]	[0.0072]	[0.0005]
Num Already Launched (Sweden, Netherlands)	0.5079***	0.6167***	0.3935***	0.3492**	0.0245***	0.0005*	0.0239***	0.0009*
	[0.0705]	[0.1548]	[0.0749]	[0.1436]	[0.0052]	[0.0003]	[0.0059]	[0.0005]
Num Already Launched (Italy, France)	0.2688***	0.0334	0.3057***	0.0945	0.0126**	0.0000	0.0185***	0.0002
	[0.0986]	[0.1192]	[0.0840]	[0.1364]	[0.0055]	[0.0001]	[0.0058]	[0.0004]
Num Already Launched (Spain,	0.0670	0.2820***	-0.0409	0.1621*	0.0031	0.0002**	-0.0024	0.0004

Portugal, Greece)	[0.0661]	[0.1038]	[0.0654]	[0.0950]	[0.0030]	[0.0001]	[0.0040]	[0.0003]
Num Already Launched (Canada, Japan, Switzerland, USA)	0.1907***	0.0034	0.1321**	-0.0844	0.0089***	0.0000	0.0079**	-0.0002
	[0.0637]	[0.1011]	[0.0560]	[0.1048]	[0.0030]	[0.0001]	[0.0035]	[0.0003]
Any PI Share in Subclass D.V.	0.0161	-0.1603	0.0670	-0.1269	0.0008	-0.0001	0.0041	-0.0003
	[0.1536]	[0.4589]	[0.1510]	[0.3596]	[0.0072]	[0.0003]	[0.0092]	[0.0009]
Launch by Local Originator Corporation D.V.	1.3954***	2.5515***	1.5681***	3.0584***	0.1286***	0.0080*	0.1822***	0.0274***
	[0.2676]	[0.2759]	[0.1626]	[0.2261]	[0.0458]	[0.0042]	[0.0420]	[0.0104]
Launch by Solo Licensee Corporation D.V.	0.5481***	1.3352***	0.5646***	1.1030***	0.0328**	0.0020*	0.0424***	0.0042**
	[0.1765]	[0.2071]	[0.1551]	[0.1928]	[0.0130]	[0.0011]	[0.0157]	[0.0018]
Launch by Local Co-marketer Corporation D.V.	0.5592***	1.6151***	0.3463*	1.1864***	0.0340**	0.0029	0.0239	0.0048*
	[0.1786]	[0.5425]	[0.1984]	[0.3468]	[0.0145]	[0.0026]	[0.0160]	[0.0028]
USD to (ECU or Euro) Exchange Rate	0.0945	-0.1796	-0.1920	-0.9665*	0.0044	-0.0001	-0.0115	-0.0025
	[0.4523]	[0.5755]	[0.4216]	[0.5723]	[0.0209]	[0.0004]	[0.0255]	[0.0017]
UK D.V.	-0.2430	0.1925	-0.1616	0.2704	-0.0101	0.0002	-0.0090	0.0008
	[0.2096]	[0.3408]	[0.2000]	[0.3605]	[0.0085]	[0.0003]	[0.0111]	[0.0010]
Netherlands D.V.	-0.8790***	0.6443*	-0.7894***	0.7236*	-0.0276***	0.0007	-0.0343***	0.0024*
	[0.2465]	[0.3618]	[0.2194]	[0.3934]	[0.0082]	[0.0005]	[0.0106]	[0.0015]
Sweden D.V.	-0.7520**	-0.0208	-0.5688**	0.1684	-0.0249**	0.0000	-0.0269**	0.0005
	[0.2968]	[0.4805]	[0.2307]	[0.4521]	[0.0099]	[0.0003]	[0.0116]	[0.0012]
France D.V.	-1.2645***	-0.7394	-1.2202***	-0.5880	-0.0340***	-0.0004	-0.0452***	-0.0012
	[0.2103]	[0.5553]	[0.2304]	[0.5148]	[0.0078]	[0.0004]	[0.0110]	[0.0012]
Greece D.V.	-1.2725***	0.8260	-1.0673***	1.0116*	-0.0341***	0.0009	-0.0418***	0.0038*
	[0.2637]	[0.5778]	[0.2496]	[0.5260]	[0.0086]	[0.0006]	[0.0116]	[0.0020]
Italy D.V.	-0.9829***	0.0104	-0.8500***	0.1479	-0.0296***	0.0000	-0.0361***	0.0004
	[0.2439]	[0.5519]	[0.2173]	[0.4900]	[0.0084]	[0.0004]	[0.0109]	[0.0013]
Portugal D.V.	-1.9128***	0.0829	-1.7246***	0.2123	-0.0405***	0.0001	-0.0536***	0.0006
	[0.2319]	[0.6012]	[0.2522]	[0.5390]	[0.0084]	[0.0004]	[0.0115]	[0.0015]
Spain D.V.	-0.8052***	0.1745	-0.6327***	0.2515	-0.0261***	0.0001	-0.0292***	0.0007
	[0.2007]	[0.5481]	[0.2181]	[0.5054]	[0.0079]	[0.0004]	[0.0112]	[0.0014]
Canada D.V.	-1.0640***	-0.5232	-0.9515***	-0.3179	-0.0310***	-0.0003	-0.0389***	-0.0007
	[0.2341]	[0.5649]	[0.2103]	[0.4931]	[0.0084]	[0.0004]	[0.0108]	[0.0012]
Japan D.V.	-2.4793***	-0.0753	-2.5477***	-0.0787	-0.0436***	-0.0001	-0.0613***	-0.0002
	[0.2353]	[0.6375]	[0.2339]	[0.4660]	[0.0083]	[0.0004]	[0.0114]	[0.0012]
Switzerland D.V.	-1.0800***	-0.3521	-0.9100***	-0.2888	-0.0313***	-0.0002	-0.0378***	-0.0007
	[0.2644]	[0.5853]	[0.2540]	[0.5726]	[0.0089]	[0.0004]	[0.0119]	[0.0014]
USA D.V.	-0.9119***	-1.2651**	-0.9440***	-1.3975***	-0.0283***	-0.0005	-0.0387***	-0.0022**

	[0.2876]	[0.6150]	[0.2336]	[0.4889]	[0.0085]	[0.0003]	[0.0104]	[0.0011]
Brazil D.V.	-1.1626***	0.3617	-0.9768***	0.5353	-0.0326***	0.0003	-0.0395***	0.0017
	[0.2411]	[0.5740]	[0.2211]	[0.4874]	[0.0084]	[0.0005]	[0.0111]	[0.0014]
Mexico D.V.	-1.3041***	0.1336	-1.1008***	0.4037	-0.0345***	0.0001	-0.0426***	0.0012
	[0.2765]	[0.6370]	[0.2448]	[0.5370]	[0.0086]	[0.0005]	[0.0115]	[0.0015]
Constant	-1.1015	-5.6436***	-1.6217	-5.7109***				
	[0.9652]	[1.7327]	[1.0217]	[1.6644]				
Therapeutic Class Fixed Effects Included?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Num Observations	23,400	96,041	23,400	96,041	23,400	96,041	23,400	96,041
Number of Molecule-level Clusters	111	239	111	239	111	239	111	239
Model Log-Likelihood	-3071.2	-2007.6	-3045.7	-1963.4				
Mean of Dependent Variable	0.0378	0.0041	0.0378	0.0041	0.0378	0.0041	0.0378	0.0041

Standard errors in brackets
* significant at 10%; ** significant at 5%; *** significant at 1%
Note: All prices are ex manufacturer prices per standard unit in 2003 US Dollars

Table 6. Marginal Effects of Prior Foreign Launch on Launch Hazard in Low-Price EU Countries for Superior Subclasses (Standard Errors in Brackets)

Marginal Effects of Prior Foreign Launch in Low-Price EU Countries Clog-log with Robust Clustered SEs	
Net effect of a Single Prior Launch in a High-Price EU Country	0.0018*** [0.0004]
Net effect of a Single Prior Launch in a Low-Price EU Country	0.0005*** [0.0002]
Difference	0.0013*** [0.0003]
Net effect of a Single Prior Launch in a High-Price EU Country	0.0018*** [0.0004]
Net effect of a Single Prior Launch in a High-Price non-EU Country	0.0006*** [0.0002]
Difference	0.0012*** [0.0004]

Standard errors in brackets
* significant at 10%; ** significant at 5%; *** significant at 1%

Table 7. Marginal Effects of Launch by a Local Corporation (Standard Errors in Brackets)

	Superior Subclasses			Inferior Subclasses		
Country	Country-specific Net Effect	# Launches by Any Local Corporation	Mean Quarterly Hazard	Country-specific Net Effect	# Launches by Any Local Corporation	Mean Quarterly Hazard
Germany	0.0121	11	6.3%	0.0030	6	0.3%
	[0.0162]			[0.0024]		
UK	0.0446	10	4.4%	0.0029*	7	0.4%
	[0.0346]			[0.0017]		
Netherlands	N/A	0	4.4%	0.0140	1	0.2%
				[0.0222]		
Sweden	-0.0107	3	3.7%	0.0054	1	0.3%
	[0.0070]			[0.0042]		
France	0.0316***	11	3.2%	0.0009	6	0.3%
	[0.0111]			[0.0008]		
Greece	N/A	0	3.4%	0.0031	1	0.5%
				[0.0057]		
Italy	0.0145**	21	4.5%	0.0040*	9	0.5%
	[0.0069]			[0.0023]		
Spain	0.0110**	4	4.3%	0.0026	5	0.4%
	[0.0056]			[0.0023]		
Portugal	-0.0001	13	2.4%	N/A	0	0.4%
	[0.0010]					
Canada	0.0058	2	3.9%	0.0008	3	0.3%
	[0.0078]			[0.0006]		
Japan	0.0092***	25	1.8%	0.0096*	31	1.0%
	[0.0029]			[0.0057]		
Switzerland	0.0448***	12	4.4%	0.0013	5	0.3%
	[0.0155]			[0.0013]		
USA	0.0097	41	5.4%	0.0008	12	0.3%
	[0.0091]			[0.0005]		
Brazil	0.0042	2	3.7%	0.0046	6	0.5%
	[0.0049]			[0.0036]		
Mexico	N/A	0	3.5%	0.0176	3	0.4%
				[0.0137]		

Standard errors in brackets

* significant at 10%; ** significant at 5%; *** significant at 1%

Note: Effects for some countries were not estimable due to an absence of launches by local corporations in those countries

Table 8. Determinants of Launch Prices, OLS and Normal Random Effects Regressions (Standard Errors in Brackets)

	OLS w/ Robust Clustered SEs				Normal Random Effects			
Variables	Superior Subclasses	Inferior Subclasses	Superior Subclasses	Inferior Subclasses	Superior Subclasses	Inferior Subclasses	Superior Subclasses	Inferior Subclasses
Superior Brands' Price Missing D.V.	-0.0615	0.0172	-0.0636	0.0252	-0.0644	0.0324	-0.0685	0.0362
	[0.1879]	[0.1199]	[0.1886]	[0.1205]	[0.1134]	[0.1114]	[0.1138]	[0.1125]
Log Avg Price of Superior Brands (Lag 1Q)	0.1574***	-0.004	0.1586***	0.0018	0.1244***	-0.0085	0.1283***	0.0032
	[0.0394]	[0.0467]	[0.0395]	[0.0480]	[0.0201]	[0.0336]	[0.0201]	[0.0336]
Inferior Brands' Price Missing D.V.	0.1093	-0.7439	0.114	-0.8025	0.004	-1.2424**	0.0157	-1.2936***
	[0.1523]	[0.7108]	[0.1541]	[0.7423]	[0.1118]	[0.4849]	[0.1121]	[0.4878]
Log Avg Price of Inferior Brands (Lag 1Q)	0.0393	0.2154***	0.0387	0.2134***	0.0844***	0.1681***	0.0830***	0.1669***
	[0.0398]	[0.0490]	[0.0397]	[0.0488]	[0.0206]	[0.0294]	[0.0206]	[0.0297]
Generics' Price Missing D.V.	0.0674	0.3731*	0.0689	0.3779*	0.0095	0.2412*	0.0115	0.2416*
	[0.1168]	[0.2001]	[0.1165]	[0.2011]	[0.0758]	[0.1236]	[0.0761]	[0.1251]
Log Avg Price of Generics in Class (Lag 1Q)	0.0292	-0.1194***	0.0294	-0.1206***	0.0169	-0.0857**	0.0162	-0.0834**
	[0.0295]	[0.0441]	[0.0296]	[0.0439]	[0.0194]	[0.0340]	[0.0195]	[0.0345]
Time Since Global Launch (Yrs)	-0.0427	-0.0245	-0.0413	-0.0264	-0.0391	-0.0077	-0.0367	-0.0114
	[0.0265]	[0.0214]	[0.0265]	[0.0215]	[0.0260]	[0.0212]	[0.0261]	[0.0212]
Time Since Global Launch Squared (Yrs)	0.0028	-0.0006	0.0027	-0.0005	0.0005	-0.0012*	0.0003	-0.0011
	[0.0018]	[0.0006]	[0.0018]	[0.0006]	[0.0018]	[0.0007]	[0.0018]	[0.0007]
First Brand Launch in Ctry-Subclass D.V.	0.1998	0.8668**	0.2034	0.8990**	0.2132	1.1729***	0.2164*	1.2199***
	[0.1656]	[0.4080]	[0.1656]	[0.4390]	[0.1307]	[0.3525]	[0.1312]	[0.3562]
Second Brand Launch in Ctry-Subclass D.V.	0.3496***	0.6166*	0.3486***	0.6076*	0.2819***	0.6197***	0.2770***	0.6406***
	[0.0824]	[0.3115]	[0.0824]	[0.3244]	[0.0749]	[0.2309]	[0.0751]	[0.2321]
Third or Fourth Brand Launch in Ctry-Subclass D.V.	0.2412***	0.3085*	0.2399***	0.3039*	0.1859***	0.2007	0.1816***	0.2066
	[0.0611]	[0.1615]	[0.0613]	[0.1631]	[0.0555]	[0.1465]	[0.0557]	[0.1471]
High-price EU Min Own Price Missing D.V.	0.2170***	-0.0523	0.2138**	-0.043	0.0649	-0.0451	0.0631	-0.0526
	[0.0821]	[0.1372]	[0.0821]	[0.1379]	[0.0575]	[0.0956]	[0.0578]	[0.0966]
Log Min Own Price in Hi-Price EU (Lag 1Q)	0.2179***	0.3905***	0.2174***	0.3960***	0.1000***	0.2746***	0.1012***	0.2847***
	[0.0623]	[0.0885]	[0.0622]	[0.0890]	[0.0261]	[0.0586]	[0.0262]	[0.0590]
Low-price EU Min Own Price Missing D.V.	-0.0185	-0.0755	-0.0161	-0.0733	0.0251	0.0545	0.03	0.051
	[0.0524]	[0.1262]	[0.0527]	[0.1259]	[0.0483]	[0.1028]	[0.0485]	[0.1039]
Log Min Own Price in Low-Price EU (Lag 1Q)	-0.0243	-0.1086	-0.0234	-0.101	-0.0221	-0.1095	-0.0188	-0.1113
	[0.0394]	[0.1196]	[0.0390]	[0.1184]	[0.0279]	[0.0790]	[0.0280]	[0.0797]

High-price non-EU Min Own Price	0.1054	-0.3101***	0.1076	-0.3195***	0.1019*	-0.1126	0.1049*	-0.1244
Missing D.V.	[0.0649]	[0.1100]	[0.0651]	[0.1112]	[0.0554]	[0.0926]	[0.0556]	[0.0936]
Log Min Own Price in Hi-Price non-EU (Lag 1Q)	0.2682***	0.0482	0.2677***	0.0532	0.1433***	-0.0278	0.1425***	-0.0197
	[0.0522]	[0.0661]	[0.0519]	[0.0640]	[0.0251]	[0.0564]	[0.0252]	[0.0570]
Any PI Share in Subclass D.V.	0.022	-0.5218**	0.0232	-0.4815**	0.0207	-0.4798***	0.0236	-0.4662***
	[0.0795]	[0.2029]	[0.0786]	[0.2134]	[0.0650]	[0.1710]	[0.0653]	[0.1732]
Log GDP per Capita	0.862	2.8591*			1.8350**	3.1564***		
	[0.9232]	[1.5889]			[0.7426]	[1.1628]		
Launch by Local Originator Corporation D.V.	0.0311	-0.2572*	0.0332	-0.2823*	0.0693	-0.1825	0.0739	-0.2207*
	[0.1009]	[0.1541]	[0.1011]	[0.1551]	[0.0694]	[0.1146]	[0.0696]	[0.1148]
Launch by Solo Licensee Corporation D.V.	-0.0742	-0.1455	-0.0708	-0.1377	-0.0543	-0.0178	-0.0452	-0.0126
	[0.0770]	[0.1246]	[0.0768]	[0.1238]	[0.0623]	[0.0940]	[0.0625]	[0.0951]
Launch by Local Co-marketer Corporation D.V.	0.0031	-0.1025	0.0038	-0.1282	0.0265	-0.1417	0.0288	-0.1679
	[0.0971]	[0.1908]	[0.0980]	[0.1937]	[0.0782]	[0.1457]	[0.0785]	[0.1470]
USD to (ECU or Euro) Exchange Rate	-0.1475	2.4535**	-0.1373	2.2873**	-0.0265	1.7490**	0.0042	1.5484*
	[0.6339]	[1.0738]	[0.6234]	[1.0742]	[0.4524]	[0.8151]	[0.4542]	[0.8220]
Country-Specific Quarterly Producer Price Index	-0.0089**	0.002	-0.0065	0.0101	-0.0088**	-0.0122*	-0.0038	-0.0021
	[0.0044]	[0.0083]	[0.0039]	[0.0064]	[0.0044]	[0.0067]	[0.0039]	[0.0056]
Avg Pack Size (Up to 100)	-0.0118***	-0.0102***	-0.0118***	-0.0100***	-0.0094***	-0.0093***	-0.0093***	-0.0093***
	[0.0017]	[0.0025]	[0.0017]	[0.0025]	[0.0010]	[0.0017]	[0.0010]	[0.0017]
Pack Size > 100 D.V.	-1.1996***	-1.6199***	-1.2014***	-1.5868***	-0.9891***	-1.4086***	-0.9930***	-1.4137***
	[0.1880]	[0.2118]	[0.1888]	[0.2062]	[0.1114]	[0.1754]	[0.1118]	[0.1773]
Avg Pill Strength (g)	0.4791*	0.0507	0.4928**	0.045	0.0577	0.1877	0.0766	0.1844
	[0.2452]	[0.0701]	[0.2457]	[0.0704]	[0.2737]	[0.1440]	[0.2738]	[0.1437]
Form: Oral Solid Delayed D.V.	-0.1014	-0.191	-0.1092	-0.1573	0.1059	0.0933	0.0926	0.0949
	[0.1994]	[0.1444]	[0.1988]	[0.1452]	[0.1823]	[0.1567]	[0.1829]	[0.1582]
Form: Injectable D.V.	2.0793***	1.7450***	2.0865***	1.7304***	1.7654***	1.9669***	1.7827***	1.9652***
	[0.3009]	[0.3579]	[0.3025]	[0.3570]	[0.0885]	[0.2165]	[0.0887]	[0.2185]
Form: Other	-0.0523	0.3387***	-0.0551	0.3414***	0.0793	0.0856	0.0734	0.0754
	[0.1683]	[0.1087]	[0.1663]	[0.1101]	[0.1702]	[0.1270]	[0.1708]	[0.1278]
UK D.V.	-0.3218***	-0.1577	-0.2751***	-0.0316	-0.2829***	-0.1225	-0.1861**	0.0103
	[0.0957]	[0.1238]	[0.0827]	[0.1202]	[0.0875]	[0.1532]	[0.0784]	[0.1472]
Netherlands D.V.	-0.0707	0.0041	-0.0734	-0.0454	-0.0669	-0.0277	-0.0711	-0.0781
	[0.1034]	[0.1372]	[0.1022]	[0.1291]	[0.0798]	[0.1557]	[0.0802]	[0.1568]
Sweden D.V.	-0.1746	-0.1626	-0.0541	0.2208	-0.3307**	-0.3624	-0.0743	0.0489
	[0.1684]	[0.2808]	[0.0859]	[0.2142]	[0.1335]	[0.2211]	[0.0844]	[0.1645]

France D.V.	-0.2055*	-0.7264***	-0.2382**	-0.8051***	-0.1272	-0.6820***	-0.1956**	-0.8015***
	[0.1117]	[0.2689]	[0.1098]	[0.2668]	[0.1003]	[0.2275]	[0.0969]	[0.2264]
Greece D.V.	0.2805	1.2931	-0.3932***	-0.8704***	1.1945**	1.6279*	-0.2393**	-0.7916***
	[0.7187]	[1.2267]	[0.1198]	[0.2541]	[0.5893]	[0.9173]	[0.1050]	[0.2231]
Italy D.V.	-0.19	-0.286	-0.3485***	-0.7525***	0.0835	-0.0639	-0.2521***	-0.6007***
	[0.1922]	[0.3790]	[0.1031]	[0.2579]	[0.1664]	[0.2958]	[0.0970]	[0.2237]
Portugal D.V.	0.373	1.4824	-0.3098***	-0.7693***	1.2153**	1.8910**	-0.2341**	-0.6161***
	[0.7279]	[1.2936]	[0.1107]	[0.2566]	[0.5961]	[0.9494]	[0.1077]	[0.2260]
Spain D.V.	0.1941	0.8328	-0.2498**	-0.6269***	0.7733**	0.9693	-0.1710*	-0.6661***
	[0.4840]	[0.8717]	[0.0992]	[0.2389]	[0.3931]	[0.6412]	[0.0928]	[0.2222]
Canada D.V.	0.0439	-0.2773	0.0363	-0.2971	0.0338	-0.2256	0.0197	-0.2684
	[0.1078]	[0.2963]	[0.1054]	[0.3000]	[0.0923]	[0.2247]	[0.0925]	[0.2273]
Japan D.V.	0.1482	-0.965	0.5852***	0.5110*	-0.3752	-1.0523	0.5573***	0.5585**
	[0.5017]	[0.8135]	[0.2021]	[0.2901]	[0.3967]	[0.6419]	[0.1221]	[0.2475]
Switzerland D.V.	-0.1417	-1.6358**	0.2091**	-0.4370*	-0.6109*	-1.5100***	0.1389	-0.2329
	[0.4039]	[0.6852]	[0.0911]	[0.2507]	[0.3162]	[0.5209]	[0.0888]	[0.2234]
United States D.V.	0.1838	-0.8207	0.5272***	0.3319	-0.35	-1.0079**	0.3833***	0.2312
	[0.4014]	[0.6421]	[0.1347]	[0.2545]	[0.3125]	[0.5095]	[0.0987]	[0.2295]
Brazil D.V.	1.2852	4.733	-0.3136***	-0.5128**	3.1815**	5.3703**	-0.2182**	-0.4591**
	[1.6940]	[2.9427]	[0.1111]	[0.2464]	[1.3787]	[2.1576]	[0.0940]	[0.2198]
Mexico D.V.	0.9276	2.9574	-0.2477**	-0.9032***	2.3375**	3.4723**	-0.1610*	-0.8161***
	[1.2631]	[2.1732]	[0.1215]	[0.2317]	[1.0153]	[1.5948]	[0.0960]	[0.2294]
Constant	-7.0696	-30.4859*	1.2244	-2.7327*	-16.8192**	-31.7366***	0.8265	-1.0996
	[8.7738]	[15.4844]	[0.8798]	[1.5754]	[7.1791]	[11.3552]	[0.7247]	[1.1956]
Log GDP per Capita Included?	Yes	Yes	No	No	Yes	Yes	No	No
Year Fixed Effects Included?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Observations	950	423	950	423	950	423	950	423
Number of Molecule-level Clusters	109	123	109	123	109	123	109	123
R-squared	0.89	0.79	0.89	0.79	0.87	0.76	0.87	0.76
Mean of Dependent Variable	0.74	-0.39	0.74	-0.39	0.74	-0.39	0.74	-0.39

Standard errors in brackets

* significant at 10%; ** significant at 5%; *** significant at 1%

Note: All prices are ex manufacturer prices per standard unit in 2003 US Dollars

Table 9. Spillover Effects of Own Price on Launch Price in Low-Price EU Countries for Superior Subclasses

Marginal Effects of Log Min Own Price on Launch Price in Low-Price EU Countries

	OLS w/ Robust Clustered SEs	Normal Random Effects
Net effect of Log Min Own Price in High-Price EU Countries (Lag 1Q)	0.4236***	0.2508***
	[0.0861]	[0.0845]
Net effect of Log Min Own Price in Low-Price EU Countries (Lag 1Q)	0.0366	-0.0096
	[0.0591]	[0.0432]
Difference	0.3870***	0.2604**
	[0.1103]	[0.1055]
Net effect of Log Min Own Price in High-Price EU Countries (Lag 1Q)	0.4236***	0.2508***
	[0.0861]	[0.0845]
Net effect of Log Min Own Price in High-Price non-EU Countries (Lag 1Q)	0.0551	0.0096
	[0.0837]	[0.0778]
Difference	0.3684**	0.2411
	[0.1641]	[0.1580]

Standard errors in brackets

* significant at 10%; ** significant at 5%; *** significant at 1%

Note: All prices are ex manufacturer prices per standard unit in 2003 US dollars

Appendix Table A1. Descriptive Statistics for Launch Model Variables

	Superior Subclasses		Inferior Subclasses	
Variable Description	Mean	Std. Dev.	Mean	Std. Dev.
New Launch D.V.	0.04	0.19	0.00	0.06
Log Avg Price of Superior Brand Drugs (Lag 1Q)	0.52	1.33	0.68	1.47
Log Avg Price of Inferior Brand Drugs (Lag 1Q)	-0.54	1.29	-0.48	1.46
Log Total Volume of All Drugs In (Lag 1Q)	12.68	1.75	12.94	1.69
Num Generic Manufs per Molc in Superior Sub (Lag 1Q)	5.08	10.30	4.41	9.27
Num Generic Manufs per Molc in Inferior Sub (Lag 1Q)	28.95	37.17	35.80	41.52
No Molecules in Superior Sub D.V.	0.05	0.22	0.05	0.23
No Molecules in Inferior Sub D.V.	0.01	0.07	0.01	0.07
Time Since Molecule Global Launch (Years)	4.41	3.97	14.70	11.88
Time Since Molecule Global Launch Squared	35.20	56.96	357.07	739.83
First Global Launch Before 1990 D.V.	0.21	0.40	0.72	0.45
First Global Launch In [1990-1995] D.V.	0.38	0.48	0.20	0.40
First Global Launch In [1996-2002] D.V.	0.42	0.49	0.08	0.26
Num Already Launched (UK, Germany)	0.69	0.82	0.51	0.73
Num Already Launched (Italy, France)	0.51	0.72	0.48	0.70
Num Already Launched (Sweden, Netherlands)	0.56	0.78	0.30	0.61
Num Already Launched (Spain, Portugal, Greece)	0.58	0.94	0.58	0.91
Num Already Launched (Canada, Japan, Switzerland, USA)	1.18	0.94	1.01	0.95
Any PI Share In Subclass- D.V.	0.16	0.36	0.22	0.41
Launch by Local Originator Corporation D.V.	0.02	0.13	0.02	0.15
Launch by Solo Licensee Corporation D.V.	0.04	0.19	0.03	0.16
Launch by Local Co-marketer Corporation D.V.	0.01	0.11	0.00	0.04
USD to (ECU or Euro) Exchange Rate	1.09	0.13	1.11	0.14
Germany D.V.	0.05	0.22	0.05	0.23
UK D.V.	0.06	0.23	0.06	0.25
Netherlands D.V.	0.06	0.25	0.06	0.25
Sweden D.V.	0.06	0.24	0.08	0.27
France D.V.	0.07	0.26	0.07	0.25
Greece D.V.	0.07	0.25	0.07	0.26
Italy D.V.	0.06	0.23	0.06	0.23
Portugal D.V.	0.09	0.28	0.07	0.25
Spain D.V.	0.06	0.24	0.06	0.25
Canada D.V.	0.07	0.25	0.07	0.26
Japan D.V.	0.10	0.30	0.05	0.21
Switzerland D.V.	0.06	0.24	0.07	0.25
US D.V.	0.06	0.23	0.07	0.26
Brazil D.V.	0.07	0.25	0.08	0.27
Mexico D.V.	0.07	0.26	0.07	0.26
Anti-asthma D.V.	0.05	0.21	0.16	0.37
Anti-clotting D.V.	0.07	0.25	0.10	0.29
Anti-depressants D.V.	0.09	0.29	0.09	0.28
Epileptics D.V.	0.15	0.36	0.03	0.16
Anti-hypertensives D.V.	0.21	0.41	0.17	0.38

Anti-nausea D.V.	0.07	0.26	0.04	0.21
Parkinsons D.V.	0.05	0.22	0.01	0.11
Anti-psychotic D.V.	0.05	0.22	0.01	0.12
Anti-ulcerant D.V.	0.11	0.32	0.09	0.28
Lipid-lowering D.V.	0.04	0.20	0.05	0.22
Migraine D.V.	0.03	0.17	0.03	0.17
Osteoporosis D.V.	0.08	0.26	0.22	0.41
Sample Size	23,400		96,041	

Note: All prices are ex manufacturer prices per standard unit in 2003 US Dollars

Appendix Table A2. Descriptive Statistics for Price Model Variables

Variable Description	Superior Subclasses Mean	Superior Subclasses Std. Dev.	Inferior Subclasses Mean	Inferior Subclasses Std. Dev.
Log of Price in 2003 USD per SU	0.74	1.65	-0.39	1.31
Price in 2003 USD per SU	27.95	150.13	7.10	46.63
Superior Brands' Price Missing D.V.	0.08	0.28	0.13	0.33
Log Avg Price of Superior Brands (Lag 1Q)	0.66	1.39	0.29	1.27
Inferior Brands' Price Missing D.V.	0.02	0.14	0.01	0.11
Log Avg Price of Inferior Brands (Lag 1Q)	-0.53	1.41	-0.55	1.40
Generics' Price Missing D.V.	0.11	0.32	0.12	0.33
Log Avg Price of Generics In Class (Lag 1Q)	-1.23	1.05	-1.06	1.11
Time Since Global Launch (Years)	2.16	2.49	6.54	7.32
Time Since Global Launch Squared	10.87	30.65	96.22	211.51
First Brand Launch in Ctry-Subclass D.V.	0.11	0.31	0.01	0.12
Second Brand Launch in Ctry-Subclass D.V.	0.15	0.36	0.03	0.17
Third or Fourth Brand Launch in Ctry-Subclass D.V.	0.30	0.46	0.11	0.31
Fifth or Later Brand Launch in Ctry-Subclass D.V.	0.44	0.50	0.85	0.36
High-price EU Min Own Price Missing D.V.	0.24	0.43	0.37	0.48
Log Min Own Price in Hi-Price EU (Lag 1Q)	0.41	1.33	-0.31	1.02
Low-price EU Min Own Price Missing D.V.	0.47	0.50	0.43	0.50
Log Min Own Price in Low-Price EU (Lag 1Q)	0.12	0.90	-0.55	0.72
High-price non-EU Min Own Price Missing D.V.	0.29	0.45	0.50	0.50
Log Min Own Price in Hi-Price non-EU (Lag 1Q)	0.60	1.45	-0.31	0.89
Any PI Share In Ctry-Subclass D.V.	0.16	0.36	0.18	0.38
Log GDP per Capita (in 2000 USD 000s)	9.71	0.66	9.60	0.73
Launch by Local Originator Corporation D.V.	0.07	0.26	0.11	0.32
Launch by Solo Licensee Corporation D.V.	0.07	0.26	0.11	0.31
Launch by Local Co-marketer Corporation D.V.	0.05	0.21	0.05	0.22
USD to (ECU or Euro) Exchange Rate	1.12	0.13	1.15	0.13
Country-Specific Quarterly Producer Price Index	95.14	6.84	93.52	9.46
Avg Pack Size (Up to 100)	33.01	28.15	31.42	27.18
Avg Pack Size > 100 D.V.	0.05	0.23	0.15	0.36
Avg Pill Strength	0.08	0.13	0.09	0.29
Form Oral Instant D.V.	0.85	0.35	0.67	0.47
Form Oral Delayed D.V.	0.01	0.09	0.06	0.24
Form Injectable D.V.	0.11	0.31	0.05	0.23
Form Other D.V.	0.03	0.17	0.21	0.41
Germany D.V.	0.08	0.27	0.05	0.21
UK D.V.	0.07	0.25	0.10	0.31
Netherlands D.V.	0.06	0.24	0.05	0.22
Sweden D.V.	0.07	0.26	0.05	0.22
France D.V.	0.06	0.24	0.06	0.24
Greece D.V.	0.06	0.24	0.10	0.30
Italy D.V.	0.07	0.26	0.07	0.26
Portugal D.V.	0.05	0.22	0.07	0.25
Spain D.V.	0.06	0.23	0.05	0.22
Canada D.V.	0.07	0.25	0.05	0.22
Japan D.V.	0.05	0.21	0.11	0.31

Switzerland D.V.	0.07	0.26	0.06	0.24
USA D.V.	0.08	0.27	0.05	0.23
Brazil D.V.	0.07	0.25	0.05	0.23
Mexico D.V.	0.07	0.25	0.07	0.25
Year 1992 D.V.	0.07	0.25	0.13	0.33
Year 1993 D.V.	0.07	0.25	0.14	0.34
Year 1994 D.V.	0.07	0.25	0.09	0.29
Year 1995 D.V.	0.08	0.27	0.07	0.26
Year 1996 D.V.	0.08	0.28	0.11	0.32
Year 1997 D.V.	0.13	0.34	0.15	0.35
Year 1998 D.V.	0.15	0.36	0.07	0.25
Year 1999 D.V.	0.10	0.30	0.04	0.21
Year 2000 D.V.	0.09	0.28	0.07	0.25
Year 2001 D.V.	0.07	0.25	0.06	0.23
Year 2002 D.V.	0.05	0.22	0.05	0.23
Year 2003 D.V.	0.05	0.21	0.03	0.16
Sample Size	950		423	

Note: All prices are ex manufacturer prices per standard unit in 2003 US Dollars

Appendix Table A3. Number of Launches, and Mean and Median In-Country Launch Delay by Domestic Status of Corporation

	Local Originator Corporations			Solo Licensee Corporations			Local Co-marketer Corporations			Non-local Corporations		
Country	Molecules Launched in Country	Mean Launch Delay in Country (Mos)	Median Launch Delay in Country (Mos)	Molecules Launched in Country	Mean Launch Delay in Country (Mos)	Median Launch Delay in Country (Mos)	Molecules Launched in Country	Mean Launch Delay in Country (Mos)	Median Launch Delay in Country (Mos)	Molecules Launched in Country	Mean Launch Delay in Country (Mos)	Median Launch Delay in Country (Mos)
Superior Molecules												
Germany	4	5.3	4	10	19.0	19	3	30.3	15	71	18.2	11
U.K.	11	4.3	1	7	11.1	0	0	N/A	N/A	62	18.2	8.5
Netherlands	0	N/A	N/A	0	N/A	N/A	0	N/A	N/A	73	16.5	10
Sweden	3	22.0	0	1	7.0	7	0	N/A	N/A	73	17.0	8
France	11	11.5	4	5	32.6	30	3	16.0	15	50	29.5	27
Greece	0	N/A	N/A	0	N/A	N/A	0	N/A	N/A	72	28.0	21
Italy	1	0.0	0	13	23.5	21	14	17.1	13	48	25.4	20.5
Portugal	0	N/A	N/A	2	66.5	66.5	2	38.5	38.5	58	32.1	31
Spain	2	0.0	0	5	24.0	21	7	25.7	18	62	29.4	23
Canada	0	N/A	N/A	3	34.0	35	0	N/A	N/A	70	27.2	14.5
Japan	17	1.8	0	6	59.2	53	11	49.2	44	19	53.0	47
Switzerland	11	10.3	5	4	48.8	11	0	N/A	N/A	63	21.5	18
U.S.A.	30	7.8	1.5	20	24.3	9	0	N/A	N/A	36	23.8	9.5
Brazil	0	N/A	N/A	2	17.5	17.5	0	N/A	N/A	68	31.0	21
Mexico	0	N/A	N/A	0	N/A	N/A	0	N/A	N/A	72	27.3	17
Inferior Molecules												
Germany	26	11.4	0	22	52.2	30.5	4	23.0	19	79	31.8	16
U.K.	18	6.7	0	11	51.6	22	1	103.0	103	86	47.6	26
Netherlands	2	55.5	55.5	3	19.3	0	0	N/A	N/A	106	38.3	19.5
Sweden	0	N/A	N/A	3	112.3	78	0	N/A	N/A	79	52.8	29
France	19	11.2	0	16	91.8	70	2	40.5	40.5	67	49.5	33
Greece	0	N/A	N/A	2	148.5	148.5	0	N/A	N/A	99	76.5	42
Italy	11	2.0	0	25	60.0	36	13	35.7	23	78	54.3	44

Portugal	0	N/A	N/A	5	49.0	51	2	7.0	7	104	61.6	41
Spain	8	5.8	0	11	47.0	24	4	35.0	29	87	48.4	40
Canada	1	17.0	17	10	99.1	124.5	0	N/A	N/A	87	71.5	52
Japan	45	0.7	0	36	64.6	56	24	68.8	54.5	53	65.5	54
Switzerland	25	6.5	0	10	69.4	43.5	0	N/A	N/A	76	38.2	21
U.S.A.	29	74.4	31	33	109.9	85	1	89.0	89	34	76.9	41
Brazil	3	36.0	0	4	67.5	68	1	40.0	40	82	87.4	54
Mexico	1	0.0	0	2	122.0	122	0	N/A	N/A	98	54.6	34

Note: Sample includes all molecules present and all country launches occurring in IMS dataset through 2003

Note: Molecules with multiple local corporations in a country were assigned to a single one in the order of Local Originator, Solo Licensee or Local Co-marketer