

**Patents, Price Controls and Access to New Drugs:
How Policy Affects Global Market Entry¹**

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Abstract

Efforts to strengthen and unify the global patent system for pharmaceuticals continue to be controversial, and a similarly fraught international debate over price controls is brewing. The outcome of international negotiations and the resulting policy decisions made by each country will have many ramifications – influencing the size of future investment in medical research, the availability of the resulting therapies, how the financial burdens are distributed across countries, and finally the health of consumers. This paper considers how legal and regulatory policies affect whether new drugs are marketed in a country, and how quickly. Less than one-half of the new pharmaceutical molecules that are marketed worldwide are sold in any given country, and those that are sold are often available to consumers in one country only six or seven years after those in another. Both price regulation and intellectual property rights influence these outcomes. The analysis covers a large sample of 68 countries at all income levels and includes all drug launches over the period 1982-2002. It uses newly compiled information on legal and regulatory policy, and is the first systematic analysis of the determinants of drug launch in poor countries.

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Introduction

The international legal and regulatory environment confronting the pharmaceutical sector is in a process of upheaval. Governments, drug companies and advocacy groups have been battling for years over the type of patent rights that will be available to industry, particularly in poor countries. Sharp criticism has been directed at the intellectual property standards required of members of the World Trade Organization—standards known as Trade-Related aspects of Intellectual Property, or TRIPS, rules. The pharmaceutical industry has asserted the importance of worldwide protection to sustain research on drugs. Developing countries, for their part, have been equally adamant that patent rights should not limit their ability to produce or buy lower cost generic versions to address public health needs. In the mid-1990s, the force of the AIDS epidemic moved this controversy out of the obscure realm of trade negotiations and onto the front pages of the newspapers as a major health and development debate.

Pharmaceutical price regulation is also receiving more intense scrutiny at the international level. The United States has been actively pushing for reforms in its bilateral trade negotiations with other nations, and has accused the Europeans and Canadians of using their price control systems to free-ride on U.S. consumers.² These pressures may well generate future reforms on a broad scale.

The choices made by each country about its patent system and price regulation will have many ramifications – influencing the size of future investment in medical research, the availability of the resulting therapies, how the financial burdens are distributed across countries, and finally the health of consumers. We focus here specifically on how those policy choices affect whether new drugs are marketed in a country, and how quickly.

Remarkably, less than one-half of the new pharmaceutical molecules marketed worldwide are sold in any given country – whether rich or poor. Some may be rejected by local health authorities, but more often no firm decides to invest in the launch. Even those drugs that are eventually marketed in one country often appear on pharmacy shelves only six or seven years after becoming available to consumers elsewhere.³ Both price regulation and intellectual property rights influence these outcomes.

When a firm is deciding whether to introduce a new product into a particular market, there are both local and global issues for it to consider. Before selling a pharmaceutical product in any given country, a firm must obtain marketing approval from the local drug regulatory authority and also

² See, for example, the speech by Mark McClellan, then Commissioner of the U.S. FDA, before the First International Colloquium on Generic Medicine. September 25, 2003, Cancun, Mexico. Available at <http://www.fda.gov/oc/speeches/2003/genericdrug0925.html> (accessed 12/28/03). Most recently, the U.S. insisted that reforms to Australia's domestic price and reimbursement system be a part of the AUS Free Trade Agreement (see www.aph.gov.au/Senate/committee/fretrade_cte for details and discussion. Accessed 1/24/05).

³ A “drug” refers to a chemical entity in any of its presentations – e.g. tablets, capsules, liquid.

educate doctors and patient groups about the drug's benefits. This can require a sizeable investment in each local market, particularly for the first entrant. Firms will not enter if they do not expect to recoup these fixed costs and they are happy to say so. Some years ago Pfizer CEO Hank McKinnell threatened that the company would withhold new treatments from France unless the government allowed higher drug prices (*Financial Times*, December 10, 2001). In the same article he claimed that many other countries could see access withdrawn, while the CEO of AstraZeneca is quoted as saying, "I think all the major pharmaceutical companies are making decisions not to launch products."

Possibly of more significance, multinationals may delay or even avoid launching drugs in lower-priced countries because they are concerned about the implications for pricing in *other* markets. Price regulators often implicitly or explicitly use cross-country comparisons to establish ceiling prices. Consumers forcefully object to paying prices that are higher than those they see being charged to consumers elsewhere, which gives firms reason to fear a political backlash if they set obviously differential prices. Legal or illegal physical arbitrage across country borders can erode prices in higher-priced markets. All of these mechanisms generate pricing externalities that affect firms' entry decisions.

Two examples are instructive. In the late 1980s, Bayer chose not to introduce its new antibiotic ciprofloxacin in India. To do so it would have needed to price the product very low to be competitive in that market, at a time when the firm was negotiating prices in its more important markets. Instead, ciprofloxacin was introduced in India three years after its world launch by the Indian firm Ranbaxy. However, eight years after the drug's global launch and long after the entrance of a multitude of local producers, Bayer also entered the Indian market (interview with Bayer executive, India, 1997). More recently, GlaxoSmithKline threatened to end its supply of products to Canada if the drugs were not prevented from leaving for the United States – where they would damage the higher prices that the firm enjoyed in that country (*Wall Street Journal*, January 22, 2003). In both situations the multinationals were clearly willing to engage in a local market at a low price. Their reluctance to do so stemmed from the potential implications for their profits in other markets.

Given the existence of international pricing spillovers one would expect to see three types of entry into poorer country markets. In some cases there will be firms interested in producing only for the local or regional market. Such firms should be willing to enter quickly at a low price (assuming that expected returns at least cover the fixed costs of entry). One might also see multinationals willing to enter poorer markets quickly in situations where they can set a price in the local market that is close to their target price in the major markets. Sales would then be limited to the local elite. Finally, as illustrated above, one might see multinationals waiting for some time after the global launch of a new product, and then finally entering the developing country markets with a low price that allowed them to capture market share.

Which of these strategies are feasible and likely will be influenced by the price regulation and intellectual property regime. Clearly strong price regulation precludes the “quick entry at a high price strategy.” Even moderate price regulation may make it difficult to recoup the fixed costs of developing a market and thus make all entry less likely.

The effect of patent law depends on its features. Patent codes distinguish between the protection of methods of manufacture (“process patents”) and the protection of pharmaceutical products (“product patents”).⁴ Process patents are a relatively weak form of protection because they do not bar other firms from entering with competing versions of a new molecule. Indeed countries have purposefully chosen to have a “process-only” patent regime for pharmaceutical innovations in order to foster a domestic industry based on inventing around originators’ manufacturing processes. India’s rejection of its adopted colonial British patent code in 1972 in favor of a system allowing only short (5-7 year) process patents for drugs is an example.

In situations where local generics firms have the capacity to copy drugs rapidly, and where even low levels of protection suffice to cover the fixed costs of initial regulatory approval and market development, a process patent system may support rapid market entry by local firms. The multinational subsidiary Glaxo India, for example, faced several competitors from the first day that it marketed its blockbuster drug ranitidine (Zantac); while Cipla was manufacturing a version of the Pfizer drug Viagra shortly after the drug’s global launch (*Wall Street Journal*, July 10, 1998).

In the debate preceding the TRIPS Agreement, however, it was argued that countries with weak patent regimes – in particular those that did not allow for the protection of pharmaceutical products – were failing to get many newer drugs because the potential for follow-on generic competition dissuaded initial entry. If the innovator firm could be assured of a local monopoly, it was suggested, it would become viable to launch more products.

But in a global market this is not obvious. Product patents indeed make the local market more attractive; but they also give control over the timing of launch to multinationals with a worldwide marketing strategy.⁵ To the extent that concern about pricing spillovers causes multinationals to hesitate, new pharmaceuticals may well reach consumers in poorer countries more slowly under a product patent regime than they would have otherwise. Consider, for example, the implications if Bayer would have had a product patent on ciprofloxacin in India. Thus it is unclear how choices regarding the patent system affect the marketing of new drugs – and we must turn to data.

⁴ Some countries also give additional protection to new formulations and new uses of existing products.

⁵ While in principle smaller local firms could develop new drugs, in fact multinationals hold almost all product patents. Some 86% of the applications for product patents in India in 1995 were submitted by inventors with a non-Indian address (CDRI, 1996) and in most developing countries the share is far higher. Going forward, as firms based in developing countries also begin to invest in the development and patenting of new products they will have the same global marketing incentives and constraints faced by the current multinationals.

There has been little empirical investigation into the determinants of drug launches. Danzon, Wang and Wang (2003) analyze launch data from 25 major markets for the years 1994-1998, and a selected sample of 85 new chemical entities (NCE). They are concerned with the effects of price regulation. Rather than trying to summarize differences in price control systems directly, they use the price for a standard unit in a drug's therapy class in an earlier year as indicator of the intensity of regulation. A similar variable is constructed for expected market size. Both higher prices and larger markets are found to have a significantly positive effect on the likelihood and speed of launch.

Kyle (2003a and 2003b) analyzes 21 OECD countries and much larger set of drug launches, including 1577 molecules developed during the period 1980-2002. She focuses primarily on how firm characteristics affect launch timing and finds, for example, that domestic firms have a 5 times higher probability of launching at home (with domestic status most important in Japan and Italy). A dummy for price regulation is included as a control variable in her estimations and is found to be significantly negative.

None of these papers consider intellectual property (IP) as a determinant of marketing decisions. McCalman (2004) provides an econometric analysis of how intellectual property might influence launch decisions – of American Hollywood movies. His data are from 1997-99 covering 37 countries, and he estimates hazard models for the effect of IP strength on the speed of film launches across countries. He finds a non-monotonic relationship with moderate IP associated with the most rapid diffusion.

This paper analyzes launch patterns across a very large sample of 68 countries over the period 1982-2002. The paper provides descriptive statistics; probit analyses of the likelihood of launch; and hazard analyses of the speed of launch. Explanatory variables include those related to the market: population, income distribution, health spending, and so on. Those of primary interest are newly constructed policy variables for the availability and strength of patent protection and the stringency of price control. This is the first analysis of pharmaceutical launch patterns that includes developing countries. Their experience is of independent interest and provides more variation in the policy variables than is found in data restricted to the OECD.

I. The Timing of Drug Approvals and Patent Protection

To understand how market entry relates to price regulation and the patent system it helps to have a clear idea of timing. Figure 1 illustrates with a very stylized example. We assume that there are two countries, the United States and a lower-income country called “Other”. An innovator firm discovers a promising new molecule and patents it in the United States. The top half of the first timeline corresponds to this patent, with time zero being the date at which the U.S. patent application was made. Following application it typically takes about 1.5 years before a patent is granted (King,

2003). Until recent harmonization to the 20 year standard agreed under TRIPS, the United States had a statutory patent term of 17 years from the grant of the patent. This would give a total expected patent term of 18.5 years. In addition, however, the U.S. has a provision to allow for an extension of the patent term on pharmaceutical products to compensate for time spent in the testing and regulatory review process.⁶ The average extension during the period of our data was about 2 years (Grabowski and Vernon, 2000), pushing the expected expiration date out to 20.5 years after application as indicated.

After having applied for a patent on its new molecule in the United States, the innovator firm has up to 12 months to submit its corresponding patent applications in other countries.⁷ The bottom half of the patent timeline tracks the firm's product patent in "Other", assuming that product patents are available there. Again time zero is the date when that the application is submitted and it falls one year later than for the U.S patent.

Applications to protect manufacturing processes may be, and often are, submitted some time after initial product patent applications. Thus there may be additional patents associated with the new product. These patents would have timelines shifted to the right of the one shown, with expiration dates further out in time. An innovative firm can effectively extend the number of years that it controls the marketing of a product if it can successfully patent all commercially feasible methods to manufacture it.⁸

Typically a pharmaceutical product patent application is made early in the R&D process. Thus, in the years following its U.S. patent application the innovator firm develops the potential product. If this stage is successful, the firm develops a dossier that describes the drug's quality and characteristics and contains reports on tests of safety and efficacy. The completed dossier is submitted to the U.S. Food and Drug Administration (U.S. FDA) for marketing approval. During the mid-1900's, the regulatory approval process took, on average, about 1.5 years (various sources in the policy references below). Although there was considerable variation, during our period of analysis the average total time elapsed to final approval in the United States was about 9 years after the initial

⁶ Introducing the option for a patent extension was one part of a larger political agreement that also allowed generic firms to enter the U.S. market by showing equivalence to an existing approved product and without repeating full clinical trials (the Drug Price Competition and Patent Term Restoration Act or "Hatch-Waxman Act" of 1984).

⁷ This period may be extended via a PCT application, but most subsequent applications are made a year later almost to the day (based on data from the Thomson Derwent World Patent Index).

⁸ This may difficult. For example, in 1991 Eli Lilly was losing molecule protection in the U.S. on its major drug cefaclor, but anticipated extending the protection of its drug on the basis of a large number of U.S. process patents. At the same time, however, the Indian firm Ranbaxy found an unpatented manufacturing process that undermined this strategy. In the words of a Ranbaxy executive, "56 processes were under patent (by Lilly in the U.S.) and we found the 57th" (personal interview, 1997).

patent application (based on the 18.5 year pre-extension term and Figures 3 and 4 in Grabowski and Vernon, 2000). Following approval, drugs enter the market directly, as indicated on the figure.⁹

The date of entry into the U.S. market represents the first global launch of the product in this illustration. The first global launch in any market is time zero in the econometric analysis and starts the lower “launch lag” timeline in the figure.

When the product enters the market in “Other” depends upon the firm attempting to market it. Most developing countries will give regulatory approval to a drug largely on the basis of a product’s acceptance by the U.S. FDA or similar E.U. authority. Thus our originator firm could submit its dossier when it makes its submission to the U.S. FDA and expect approval at more or less the same time. A generic applicant, on the other hand, would need to show equivalence to the already approved product, and this might delay its submission. On average the approvals process in developing countries during the mid-1990s was also on the order of 1.5 years (policy references). Thus, *assuming a firm makes the effort to enter quickly*, we indicate approval in “Other” as one to 1.5 years after the U.S. approval date.

In most countries, marketing approval is followed by a period during which the firm negotiates the conditions of entry with a government body charged with regulating reimbursement and pricing. This process can naturally vary in length depending on the stances taken by the negotiating parties and the procedural framework. A study of developed country markets found that the average additional delay due to price negotiations was relatively short – a few up to about ten months.¹⁰ Assuming that negotiations might be somewhat more protracted in developing countries, we indicate market entry in “Other” at year 10. This implies entry two years after the first global launch, as shown on the bottom timeline.

What these timelines highlight is that the effective life of a patent – the number of years during which a patent protects a product that is out in the market generating revenue – is typically nine or ten years shorter than the statutory term of the patent. We refer to this figure when interpreting the results below.

II. The Drug Launch Data

The launch data are drawn primarily from the December 2002 “LifeCycle: Drug Launches” database constructed by the private vendor IMS Health. The database identifies the month and year that a product first has retail sales in a given country, and indicates which entries represent first world

⁹ *Competitiveness and Performance Indicators 2001*. Pharmaceutical Industry Competitiveness Taskforce. Available at <http://www.advisorybodies.doh.gov.uk/pictf/cpi2001.pdf> (accessed 1/3/05).

¹⁰ *ibid*. Consultant and industry sources cited in Danzon *et al* (2003) suggest somewhat longer delays due to price negotiation.

launches of new chemical entities (NCE).¹¹ For each product launched, it gives the tradename, the Anatomical Therapeutic Classification (ATC) code, and composition. Coverage includes entry during the 21 years 1982-2002 in the retail sector and, for some countries, the hospital sector also. The Indian market was not covered by IMS during this period so we incorporate similar information obtained from the Indian market research company, ORG-MARG. The Indian data cover a partial, but broad, set of therapeutic classes – including launches of all antibiotics, ulcer and cancer drugs – and includes all products in those classes launched in the Indian market during the period 1986-98. The combined dataset covers 68 countries or country groups,¹² 60% of which have at least twenty years of information.

Because the brand names given to the same product change across countries, and may include generics, common products must be linked across countries on the basis of active ingredients. Although (active) “ingredient” is a variable field, it is incomplete in the IMS data, with a sizable share of the observations missing active ingredient information altogether.¹³ We assume that drugs having a tradename that is the same as one of the NCE chemicals are generics and assign to them their tradename chemical as an ingredient. After having made this change, about 10% of the observations were left with missing ingredient information. The share of launches missing this key linking variable differs considerably across countries but is not obviously related to language or income. For example, 18% of U.S. launches are missing ingredient but only 9% of Japanese and Swedish launches.

The IMS data contains a field “Composition” which includes both active and inert ingredients. Two-thirds of the observations with missing information in the ingredient field had information in the composition field. This field revealed that many of products missing information are not likely to be NCEs (for example, “charcoal”, “calf blood extract”, “acne acid detergent”). While the ingredient field typically had chemicals listed in the common chemical nomenclature, those listed in the composition field were more often in the language of the country of release (for example, “pirodoxina chlorhidrato”, “rosskastanien samen-trokenextrakt”, “prodotto a base di aglio”). To avoid introducing new noise and probably a bias associated with language, no attempt was made to use the composition

¹¹ In some cases the same chemical was indicated as being ‘new’ more than once, or was identified as ‘new’ at a country launch later than the first launch in the world. In these cases the first appearance is taken as the global launch date.

¹² French West Africa (Benin, Cameroon, Congo, Cote d’Ivoire, Gabon, Guinea, Senegal) and Central America (Costa Rica, El Salvador, Guatemala, Honduras, Panama) are aggregated by IMS because they are very small markets. During the period 1982-1992 we have data for “West Germany”, which overlaps with data for “Germany” beginning in 1989. Inspection of the entries for these two “different” countries during the overlap period reveals some drugs released in both countries and others in one or the other. These observations are treated as a single market during the overlap period. For the 1982-1988 period, IMS also reports launch information for “Malaysia”, “Singapore”, and a “Malaysia, Singapore” hybrid. Drugs released as “Malaysia, Singapore” are treated as having been launched in each country and the observations are replicated.

¹³ There was considerable improvement in reporting over time: about 1/3 of the 1980’s launch observations are missing ingredient, while the data are complete for launches in the last five years.

field to identify active ingredients where they were missing. Observations that do not have identified ingredients are dropped from the analysis except in Table 4 below.

To improve the links between common products for those observations that do have identified ingredients, we constructed a set of chemical “equivalent names” for each of the NCEs. Most of the equivalent names came from a search of an online chemical database called ChemID Plus.¹⁴ This yielded 5,374 synonyms. In addition, we found the original tradename under which each NCE was first launched, identified all products launched under each of those tradenames, and the products’ ingredients. Whenever a given NCE tradename had different ingredients listed for products in different countries, these were scrutinized to find different spellings due to language or misspellings. This resulted in a further 61 equivalent names to use for matching.

Drugs assigned to an ATC code beginning with “T” (diagnostic agents and testing devices) or “V” (various, including dietetic supplements and similar products) were dropped.

Appendix Table A1 gives an example of a launch pattern for the pharmaceutical ciprofloxacin. Countries are ordered by date of market entry. Ciprofloxacin was first marketed in the Philippines in October of 1986, so this date is time zero. The number of months between the date of the first global launch of a drug and its launch in a given country is the launch lag. These are given in the last column of the table.

III. Description of Global Launch Patterns

Table 1 gives the number of NCE’s with a first appearance (global launch date) in each year. The first column indicates the number of new “blockbusters” – drugs launched quickly in a relatively large number of major markets – and the second column includes all drugs. There was an increase in the number of new chemical entities launched in the mid-1980’s, with some fall off in the numbers in the early 2000’s (perhaps due in part to data processing delays). On the whole, however, the number of NCE’s appearing each year was fairly similar over the period.

There were 836 new pharmaceuticals first marketed during the period 1982 – 2002. Table 2 indicates the location of these first launches. The table includes countries having at least one first launch, ordered by income class.¹⁵ To have an accurate picture of the actual importance of countries as a location of first launch requires an adjustment to these figures because some countries have incomplete coverage over the period (see column 2). For example, Russia appears as the location of first launch only twice, but this is due in part to our having only eight years of information. Thus, column three gives an adjusted percentage share. It is constructed as follows. Let d_{it} be the observed

¹⁴ at <http://chem.sis.nlm.nih.gov/chemidplus/cmplxqry.html> (accessed March, 2003).

¹⁵ The income classes follow those in the World Bank 2002 *World Development Indicators Report*. The ranges for GNI per capita measured in 1999 U.S. dollars are: Low \leq \$755 < Lower \leq \$2995 < Middle \leq \$9265 < High.

number of first launches in country j in year t and D_t the observed first launches in year t worldwide. Let s_{j0} be an estimate of country j 's share of first launches based on data from the seven-year period 1995-2001 when information was available for all countries. For the remaining years, first estimate

the true number of first launches as $D_t^* = \frac{D_t}{\sum_{j \in J_t} s_{j0}}$, where J_t is the set of all countries having data in

year t . Then, for each country $j \in J_t$ construct estimates of the country's annual shares as $s_{jt} = \frac{d_{jt}}{D_t^*}$.

Each country's adjusted share of first launches over the entire period is a weighted average of s_{j0} (the share over 1995-2001) and the other annual estimates s_{jt} available for that country.

Two points stand out in this table. First, firms almost invariably launch products first in rich country markets. Second, a very large share of all drugs is launched first in Japan (and only there – see below).

Figure 2 gives an idea of the number of countries that an NCE typically reaches. It is based on the 300 NCEs with global launch dates early in the period (1982-1988) to avoid truncation. We see that only a very few drugs from that time period were launched worldwide. The mean number of countries is 20, the median is 9, and almost 20% of new drugs are marketed in just a single country. Of the 54 single-market drugs represented in this figure, 23 were sold only in Japan, 13 only in Italy, with the rest scattered across countries. Japan is clearly distinctive – it is the location of 24% of all drug launches, but 43% of those marketed in a single country. From 1995 there was a marked increase in the number of countries reached within a short span after global launch, so it is likely that today the distribution shown in Figure 2 has shifted rightward.

Table 3 indicates how long it takes for a drug to become available to a country's consumers. Calculations in this table are restricted to the 122 NCEs first launched 1986-92 and assigned to therapy classes for which the Indian data are available. There is some truncation for drugs entering after a long delay because the data end at 2002, but each NCE has at least 120 months of information. It is evident that lags tend to lengthen as one goes down the income rankings. The group summary at the bottom of the table shows that differences are most pronounced between the high-income countries and the rest.¹⁶ However, there is also clearly a great deal of variation across individual countries: median launch lags range from months (Japan, Switzerland) to over eight years (Latvia, Lebanon). There is also considerable variation across products within countries: For example, the difference between the 10th and 90th percentile of the lag distribution is over 10 years in Morocco and Peru and over 7 years in some of the OECD countries.

¹⁶ The difference for high income countries is not driven by the fact that Japan has a large number of unique drugs. Dropping Japan lowers the average number of drugs to 40 and increases the median lag to 28 months.

To avoid differing degrees of truncation across years, Table 4 restricts attention to launches that occur within 10 years of the first global launch of each NCE. The ten-year span includes most market entry, as shown in the previous table. Table 4 includes the 462 drugs in all therapy classes first launched from 1982-92 (so India is dropped). The first column, on the left side of the table, gives the percentage of this group of pharmaceuticals that is launched in the row country at any point within ten years. The second column gives the same statistic but where the launches in each country have been grossed up as though products missing ingredient information are, in fact, NCE products. As discussed in the previous section, this is clearly not the case so these values would be generous upper bounds.

Considering the first column, the percentage of drugs launched within ten years ranges from lows of 19% and 22% (Egypt, Malaysia) to highs of 49% and 53% (Italy, Japan). Thus, no consumers anywhere have access to more than about one-half of the new pharmaceuticals that enter the world market. The mean (unweighted) percentage is 34.8% for the high-income countries, and 29.9% and 28.4% for the middle- and low-income countries, respectively. The fact that drugs are not launched more widely can be due to the availability of substitutes, differences in disease patterns across countries, and rejection by some local regulatory authorities.

The remaining columns of Table 4 give the cumulative distribution of drug launches at different lags from one year to nine years. Thus the column headed “3” indicates the percentage of all NCE launched within ten years in a given row country that arrived in that market within three years. Countries are listed by income group and, looking down this column, we again see that drugs are more likely to be launched within three years in the richer countries than in the poorer countries. This is highlighted in Figure 3, which shows unweighted averages for each income group. However, the pattern is not strong. Israel, at 27%, for example, has a smaller share on the market this quickly than either the Philippines or Thailand (44% and 41% respectively). Again we see the large range of experience overall. Germany has 75% of its drugs on the market within three years of the global launch, Saudi Arabia just 16%.

To summarize the descriptive statistics:

- Only 20% to 50% of all drugs launched globally are on the market in any country after 10 years.
- Across countries there is considerable variation in how quickly drugs arrive on the market given that they are ever launched.
- There is some indication that countries with higher GDP per capita tend to obtain new drugs more quickly, but the pattern is not strong.

- Within any given country there is also considerable variation in how quickly individual drugs are launched – ranging from a few months to over a decade.

IV. The Explanatory Variables

Annual series were constructed to describe each of the main policy areas:

Intellectual Property Protection: These variables include indicator variables for the availability of patents on innovative methods of manufacture for pharmaceuticals (process patents), and patents on new pharmaceutical compounds (product patents). Historically, countries have offered either no protection in the area of pharmaceuticals, process patents only, or both process and product patents. The data include the statutory term of each form of protection, as well as information about whether a country allows for an extension to the patent term to compensate for time spent in the marketing approvals process.

How a country interprets and enforces its patent laws clearly affects how meaningful any patent “rights” are to their owners. Unfortunately this is a difficult characteristic to capture in data. We use one variable, “strong,” falling between 0 and 1, which takes on a higher value as a country limits how patent rights can be curtailed. Specifically, it is the average of non-missing values for three other 0/1 indicators: the first equals one if a country will not impose compulsory licensing until three years after patent grant; the second equals one if the country has no formal obligation to “work” a patent (supply the market); and the third equals one if the country does not revoke patents for failing to work if there is such a requirement. This variable was devised by Walter Park, who provided the data required for its construction for most countries for each five years beginning in 1980 (see Ginarte and Park, 1997, for details). For missing countries, his data were supplemented assuming current values throughout the period based on the legal texts referenced below. A similar variable composed of enforcement-related indicators was not found to have any explanatory power and therefore was not included in the estimations.

Price Control: There is bewildering variety in the ways in which different countries approach the control of pharmaceutical prices. We consider explicit price regulation and summarize the variation in countries’ systems with two dummy variables – one for the existence of “some” price control regulation and the second for “extensive” price control. A price regime is labeled “extensive” if all drugs are regulated, rather than just a subset of the market, or if a country’s price regulation is identified by commentators as being particularly rigorous. The set of reports consulted in making this determination is given in the policy section of the references.

The legal and regulatory policies of a country result from some process, and this makes endogeneity an obvious concern when trying to understand the effects of any policy regime. In our

case, one might expect firms to lobby hardest to obtain strong patent protection in countries viewed as attractive markets for entry, potentially creating a positive bias in estimated relationships.¹⁷ However, a consideration of actual events suggests that substantive within-country changes in the patent law can reasonably be treated as exogenous for our purpose – certainly in their timing. Such changes tend to be forced by the rules of entry into new political groups (e.g., Portugal and Spain joining the EU in 1992); by newly negotiated standards created at an international level (e.g., many poor countries and TRIPS, Mexico and NAFTA); or a vulnerability to trade pressure and the political dynamic of bilateral negotiations (Korea, Brazil, and Jordan in the 1980s and 1990s). (See Sell, 2003.) The link to the dynamic of trade negotiations is reflected in comments by the body that advises the U.S. Congress and administration on IPR and trade, the Industry Functional Advisory Committee on IPR for Trade Matters (IFAC-3), in its reports to the US Trade Representative:

CAFTA (the Central American Free Trade Agreement) “mirrors, as closely as possible, the Singapore and Chile FTAs in order to establish clear precedents in most key areas of intellectual property protection for *future* FTA negotiations.”

And

“IFAC-3 is particularly gratified that....with high-level agreements with both small developing countries in the CAFTA and a strong and mature developed country like Australia, it will prove much easier to convince future FTA countries that strong intellectual property protection is in the interests of all countries *regardless of their economic circumstances*.” (Italics mine).¹⁸

The timing of other reforms, such as adding a patent term extension or strengthening enforcement procedures, may be more subject to specific industry interests.

Price regulation is more likely to be endogenous. While patent laws change only rarely, and then in fairly specific and major ways, governments more frequently adjust systems for controlling prices. Weaker regulation might be driven by pressure from an industry with an eye on entry for other reasons. There are, however, strong countervailing forces that limit industry influence, such as budgetary pressures and vigorous lobbying by patient groups and the retired elderly.

To mitigate potential endogeneity concerns and remove noise we construct controls for other characteristics that one might expect to influence pharmaceutical marketing. Some of these control

¹⁷ And lobby they do. For a candid discussion see historical issues of the PhRMA annual report.

¹⁸ Industry Functional Advisory Committee on IPR for Trade Matters (IFAC-3) in reports to the USTR: http://www.ustr.gov/assets/Trade_Agreements/Bilateral/CAFTA-DR/CAFTA_Reports/asset_upload_file571_5945.pdf and http://www.ustr.gov/assets/Trade_Agreements/Bilateral/Morocco_FTA/Reports/asset_upload_file164_3139.pdf (both accessed 12/06/04).

variables are of independent interest. Most of them relate to the potential profitability of the market and thus firms' interest in launching there. Differences in market opportunities are captured by the demographic indicators population size and the percentages of the population aged 0-14, 15-64, 65+ years. Economic variables include the level of GDP per capita. The Gini coefficient of inequality, and asset ownership, provide some measure of differences in income distributions. We also control for the share of health expenditure in GDP, and the share of health expenditure that is private.

Characteristics of the regulatory process can also influence market entry. Health authorities differ in their standards and some may reject a new drug even when it is on the market elsewhere. Delays in the marketing approvals process can take the speed of drug launch at least partially out of the hands of firms.¹⁹ The observed timing of market entry reflects some combination of the decisions of firms and the complexity and efficiency of a country's regulatory process. Thus, the estimations include other elements of government policy that might directly affect or proxy for other conditions that influence entry timing, beyond our key variables of interest. These include whether a country has adopted an essential drug list, standard treatment guidelines or a national formulary. For EU members we include an indicator of the 1995 establishment of the European Medicines Evaluation Agency. This agency offers a centralized, and thus potentially more rapid, approvals procedure within the European Union.

Given the historical link between changes in patent law and trade agreements, one might be concerned that what looks like a positive role for stronger patents could be due to other changes in the trade regime facilitating market interaction. To test this, annual exports was included as a control variable in unreported estimations. Its inclusion had little effect on the estimated coefficients on the policy variables, providing no evidence of a bias. Because inclusion of exports causes the loss of a sizeable number of observations it is not used in the estimations presented below.

Many of the explanatory variables are available annually and others are in one or several cross-sections. All variables used in the estimations presented below are defined in Appendix Table A2 with summary statistics in Table A3.

V. Econometric Analyses of Launch Determinants

This section describes the probit and hazard model estimations used to analyze the probability and speed of drug launch. Results are discussed in the following section.

¹⁹ Firms are able to influence how quickly a given drug moves through the approvals process. They can work with more institutions and offer greater compensation to participants in order to rapidly reach required sample sizes for clinical trials. They can direct more resources to interacting with the authorities during the approvals process. Dranove and Meltzer (1994) provide evidence from the United States that firm work harder to speed the approval of drugs that are later successful in the market.

All estimations are done separately for the high-income countries and for a combined low-and middle-income grouping. We consider four different subsets of the NCE in the data. The base estimations include all drugs. However, some drugs launched in one location fail to reach other country markets because they do not meet those countries' local health standards for safety or efficacy. We want to distinguish between firm's decisions not to launch, and a failure to fulfill marketing requirements. Thus, for the high-income countries we also estimate the models on a "high quality" subset of NCEs, defined as those that obtain marketing approval and are launched in either the U.S. or the U.K within 2 years. This follows Danzon, Wang and Wang (2003), who argue that these two countries have the most stringent regulation and that therefore approval for their markets implies a minimum quality standard.²⁰

For the low- and middle-income group we focus on a set of "blockbuster" drugs – those that look to be of greatest commercial importance. These are identified as drugs that are marketed in at least four countries of the European Union or United States within two years of their global launch – for drugs with a global launch before 1995 – and at least 9 countries for those first launched after that date. These cutoffs are chosen to include about twenty percent of NCE launched in each year. The group includes drugs of great medical importance and also some major "lifestyle" drugs. We examine the launch of blockbuster drugs in the low and middle-income group only, because drugs in this group are launched quickly in the rich countries by definition.

Finally, when examining launch in the lower-income group we consider separately the two therapy classes that have sales relatively more concentrated in developing countries: class A (alimentary tract and metabolism) and class J (systemic anti-infectives). The sales of drugs in class A and J were 23.6% and 23.0% of all sales in India in 2000, while only 10.4% and 18.1% of the NCE in our data fell in these therapy classes (sales figures from Chaudhuri, *et. al.*, 2004). Firms might have stronger incentive to enter poorer markets with products in these classes.²¹

Tables 5-7 and Tables 9-10 contain the estimation results for probit models of the probability that a new drug is launched in a given country within either two years or ten years of the drug's first appearance in the global market. Observations are at the level of a country/NCE and the dependent variable takes on the value one if the NCE was marketed within the indicated period of time. A 24-month lag is below the median lag for high-income countries, and below the 10th percentile for low- and middle-income countries (see Table 3). Thus, product entry within this timeframe represents

²⁰ Unlike Danzon, *et. al.*, we drop the U.S. and the U.K. as launch countries when analyzing this subset since their launch probabilities are biased upwards by construction. Another way to approach the quality issue is to restrict attention to drugs known to satisfy a given country's standards because they are observed entering its market within ten years, and analyze the probability that those drugs are launched within two years (analogous to Table 4). Unreported estimates on this subset support the results discussed below.

²¹ Virtually all drugs are also marketed in the high-income countries. Of the over four hundred NCE launched through 1992, only eight were launched exclusively in the low- and middle-income countries and only one of these in more than a single country.

relatively rapid launch, particularly in the poorer countries. As discussed in Section I, on average the procedural steps required for market entry should not cause a delay longer than two years, particularly for the originator firm (see Figure 1). Thus, if a launch fails to happen within two years one can fairly assume that this failure involved at least some element of firm choice to delay, or that a decision was made to enter but the product was rejected by the health authority. The descriptive statistics presented above suggest that a lag of ten years is a reasonable indicator of whether a drug is “ever launched”.

Table 8 contains estimation results for a log-logistic hazard model of the time path of country launches.²² The log-logistic model implies that the probability of failing to have a new drug on the market t months after the global launch is

$$S(t) = \left[1 + \left(\frac{t}{\exp\{x\beta\}} \right)^{1/\gamma} \right]^{-1}.$$

This functional form – which allows for increasing and then decreasing hazards rates through the parameter γ – was preferred over other frequently used specifications such as Cox proportional hazard or Weibull models for all subsets of the data. Comparing the empirical cumulative hazard rates and the Cox-Snell residuals revealed predicted hazards that were too high in the later years. This is reasonably explained by the fact that for each country the sample is a combination of drugs that are eventually launched – hence which are well described by the model – and those that never will be. To accommodate this unobserved heterogeneity across drugs, the estimations also allow for a multiplicative factor on individual hazards having a Gamma distribution with mean one and variance θ . This standard form yields a convenient analytical expression for the likelihood function.

In all specifications, countries enter the estimation for a given NCE only if the NCE’s global launch precedes the entry of the country into the database. To avoid truncation, the hazard estimations include NCE first launched 1982-2001, the probit estimations for a two-year lag include those first launched 1982-2000, while those for the ten-year lag include only NCE with first launch 1982-1992. All estimations include full sets of dummy variables for both the date of NCE first global launch and ATC therapeutic class. Country fixed effects are also included in some of the probit estimations – as indicated in the column headings – and in the hazard estimations. Their inclusion implies the loss of all information available from cross-country variation in the key policy variables; but focusing on within-country changes over time has the advantage of controlling for any unobserved market characteristics that might be correlated with those variables. Appendix Table A4 indicates the countries that saw changes in their policy variables during relevant time periods. Time, therapy class, and (where included) country fixed effects are each jointly significant in all cases. Where country fixed effects are not included in the model, the estimations allow for a country random effect.

²² Global launches are defined as being a launch in the first month to avoid those observations being dropped.

Explanatory variables are dated by the year of the first global launch. For example, if an NCE is first marketed in 1990 then it is a country's population size in the year 1990 that is considered as a determinant of drug launch in the period two or ten years after 1990. This is not obviously the right assumption – one might expect that the relevant characteristics would be those for a later period, particularly for the probability of launch within ten years. However, experimentation showed that both policy and market variables dated after the global launch (either two or four years) have weaker explanatory power in models of new product launch. It may be that worldwide launch decisions for a new drug are taken at the time of first marketing, or that information about changes in markets only enters firms' marketing decisions with some delay.

VI. The Estimation Results

We now examine the determinants of drug launch. Coefficient estimates on the patent regime and price control variables are discussed in detail, followed by a brief discussion of other estimates.

Low- and Middle-income Countries

Results of probit estimations for the low- and middle-income countries are presented in Tables 5 through 7, with corresponding hazard model estimates in Table 8.

The type of patent protection offered by a country in this income grouping is characterized by a set of five dummy variables (see the first rows of Table 5). Information on the length of protection is collapsed into indicator variables for whether protection is short vs. long protection. This distinction has explanatory power whereas the specific statutory term length in years does not. While somewhat surprising, launch decisions are made by managers who must synthesize different types of information and it is quite plausible that the simpler breakdown is the way in which they think about country patent policies when making their choices.

The first of the five dummy variables indicates whether a country offers at least short-term process protection for pharmaceuticals versus no protection at all (see the diagram below). For the lower-income countries "Short" refers to a statutory term of 14 years or less.²³ Recalling Figure 1, a term of 14 years would imply that, on average, about four years of effective protection would be conveyed by a patent on the product molecule and perhaps a few more years by associated process patents because of their later application dates. Of the periods in which countries in the data offered a short term of protection, in about 25% of cases the term was 14 years. In about 50% the term was 12 years, implying an average effective patent life of only a few years. In the remaining cases the term was just 7 years.

²³ Experimenting sequentially with cutoffs from 12 to 17 years, 14 gave the highest pseudo- R^2 .

The next two variables capture the *incremental* effect of moving to either to long process protection (≥ 15 years), or alternatively adding short product protection. The fourth variable indicates the additional effect of going from short protection of both products and processes to long protection of both. (One never observes a country with short product protection and long process protection.) The final dummy variable indicates whether the country will grant an extension on product patents to compensate for marketing time lost during the approvals process.

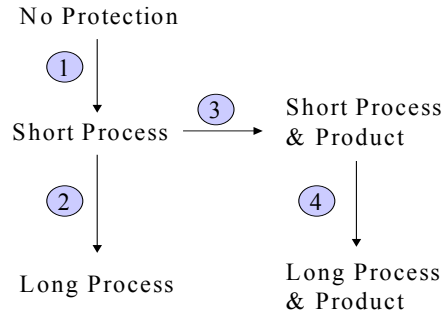


Table 5 presents results for the full set of drugs. The first model in column one includes country fixed effects, while the second and third do not. Because the latter two specifications include the Gini coefficient, a number of countries are lost due to missing information. Comparing the estimated coefficients across columns one and two (models which are the most similar) we see that the size of the estimates are reasonably robust to the assumption of fixed or random country effects.²⁴ This lends empirical support to the argument that the policy variables can be treated as exogenous.

The observed probability that a drug is launched in a low- or middle-income country within two years is about 9%. The estimates in Table 5 suggest that going from a regime with only short process patents to one with long process patents significantly encourages rapid entry. A long process patent regime still allows for possible generic entry and this appears to be important. The marginal effect is to raise the probability of launch within two years by 2-3 percentage points (or about 30%). There is little evidence, however, that offering any form of protection to new pharmaceutical products enhances the likelihood of quick entry into these markets. The incremental effects of adding short and then long product protection are insignificant in all specifications, and the combined effect is weakly significant only in the random effects models (0.021 + 0.008, p-value 0.08; 0.012 + 0.012, p-value 0.06).

Extensive price control clearly lowers the probability that new pharmaceuticals quickly reach consumers in lower-income countries, as expected. The predicted effect is similar in magnitude to that of the change to a longer term on process patents – in this case lowering the probability of rapid entry by some 30%. That a country has an essential drugs list is also associated with a lower likelihood that new drugs are launched quickly and may indicate more focused efforts by the government to ensure that drug purchases are cost effective.

Moderate price control, on the other hand, does not appear to have a significant influence on entry, unless one allows for an interaction with GDP (column 3). The results with the interaction suggest that even moderate regulation of prices will lower the likelihood that new drugs are launched quickly in the poorest countries. This finding may reflect firm choices. It might also result from poorer countries having less efficient regulatory procedures that slow price negotiations. There is some suggestion of the importance of variation in regulatory efficiency within the lower-income countries in the fact that the coefficient estimates on having adopted standard treatment guidelines and having a national formulary are significantly positive (which is not the case for the higher-income countries, see below). One would expect their direct effect to be negative, but within the low- and middle-income country group these variables may be acting as proxies for bureaucratic competence.

The point estimates indicate that moderate regulation no longer slows launch once a country reaches a GDP per capita of about \$6,800, an income level above the mean for this group but well below the ceiling of \$9,265.

The first column of Table 6 adds two new variables: interactions between short and long product patent variables and the indicator “Strong” that indicates limits on how patent rights can be curtailed. There is some evidence from these interactions that short product patents may encourage rapid entry when they are held in a legal environment more generally supportive of patentee rights. It may be, for example, that in such an environment the patent holder feels able to simply import product rather than go through the time consuming process of finding local producers and/or distributors to license.

The second and third columns of Table 6 correspond to the last column of Table 5, for the subsets of the NCE indicated in the column headings. As found for all drugs, the NCE in classes A and J (“LDC concentrated”) are more likely to be launched quickly when a country offers only long process patent protection. In addition, for this subset of NCE there is also evidence that offering long protection on pharmaceutical products can encourage rapid entry. The incremental effect of long product protection is positive and weakly significant and the estimated coefficient on having a patent

²⁴ Because there is limited variation in the policy variables – particularly when country fixed effects are included – a jackknife procedure was used to look for potential overfitting of the data. Countries were dropped in turn, the model re-estimated and the resulting coefficient estimates checked for stability.

term extension provision is both significant and sizable. Results for the other policy variables are similar to those for all drugs in Table 5.

The last set of estimates given in Table 6 is for the relatively widely marketed “blockbuster” group of NCE. For a low- and middle-income country the probability that one of these drugs is launched within two years is considerably higher than is the probability for all NCE (25% vs. 9%). That said, there is no evidence that offering any form of patent protection – whether long or short – speeds the arrival of the world’s blockbuster drugs to their markets. This finding does not seem to be an artifact of the smaller sample size, since other estimations showing significant effects of the patent variables have even smaller sample sizes. Further, the other policy variables remain significant and are estimated to have a similar-sized effect on the launch of blockbusters (relative to the observed probability) as they do for other sets of NCE. We return to this point below.

Table 7 presents results for the probability of launch within ten years. These estimations include only NCE launched globally by 1992. To enable accurate comparisons, results for launch within two years are also given for this earlier and smaller sample. The first pair of within 2 and within 10 results is for the full set of early-period NCE. There is again evidence that a long process patent regime supporting of generic entry is conducive to rapid drug launch (within 2). In this 1980’s and early 1990’s subset of the data, a long product patent regime to encourage entry by innovator firms also gives significant support to rapid entry. The fact that the benefit of product patent found here is no longer evident in the full period data (Table 5) suggests that innovator firms may have become less comfortable with the “high price, quick entry” strategy. In the early period, short process patents appear counter-productive to market entry, perhaps creating complexity while at the same time being too modest to significantly help firms to recoup fixed entry costs.

Policy choices have some notably different effects on whether drugs are “ever” launched. Contrary to the finding for rapid launch, there is only weak evidence that moving from a short to a long process patent regime increases the likelihood of a drug being marketed eventually. Instead, there is a significant benefit in the longer term associated with giving short-term protection to innovative products. The addition of short product patent protection increases the estimated probability that a drug is ever launched in a lower-income country by 5.7 percentage points (almost 20%). Interestingly too, although price regulation significantly reduces the likelihood that a drug is launched quickly, even extensive price control does not appear to reduce the likelihood that a drug is marketed eventually.

The second pair of estimates is for early-period blockbuster NCE. The same pattern of estimated effects on the patent and price control variables across the two- and ten-year timeframes is evident for this smaller set of drugs. In particular, during this early period long process patents encouraged the rapid launch of blockbusters. That this effect is lost in the more recent years (Table 6) may suggest that innovator firms have begun taking greater care to prevent generic entry of commercially promising drugs by obtaining more blocking process patents themselves.

Taken together, the findings in Table 7 suggest both that innovator firms are an important source of drug entry (hence product patents matter for eventual launch) and that these firms are, in fact, willing to enter poorer markets at low prices with only a few years of effective patent protection – after some delay. Given this, unless speed of access is paramount, a low- or middle-income country would seem not to benefit in terms of greater product availability from offering a long term of patent protection or from limiting its price control regulation.

Table 8 presents results for the hazard model. They are in an accelerated failure time form which means that a *negative* coefficient is associated with shorter launch lags and thus corresponds to a *positive* coefficient in the probit estimations. The hazard model summarizes the effect of policy on launch behavior at all monthly lags after global launch and thus incorporates - within a specific structure - both the “within two year” and “within ten year” launch probabilities. Thus it is not surprising to see in the first column of Table 8 that both increasing the term on process patents and making short protection available on new products speed drug launch.²⁵ Again we find that while extensive price regulation slows launch, moderate price regulation, on average, has no effect in this group of low- and middle-income countries. The results for the set of blockbuster drugs shown in column two of Table 8 are also similar to the corresponding estimates in Table 7.

High-income Countries

There is less variation in the patent regimes observed in the high-income countries. For example, all of the countries in this group offered at least protection on pharmaceutical processes over most of the period. Thus, for this group of countries the set of indicator variables is limited to three: a dummy for whether a country protects pharmaceutical products, another for the incremental effect of having a long statutory term on either form of protection, and finally a dummy variable indicating whether a patent term extension is available. For this group of countries, “Short” refers to a statutory term of less than 20 years, the distinction preferred by the data.

The estimations in Table 9 for the high-income countries and the full set of NCE follow the same format as Table 5. For this set of countries the estimates on the policy variables are less robust to the choice of fixed or random country effects (compare models one and two).²⁶ It may be that the policy variables are picking up some the effect of other country level characteristics in the random effects specification. However, it is also the case that among the high-income countries there is more limited within-country variation in the policy variables (see Table A4). As a result the countries

²⁵ From Table 7 it is clear that a model allowing for changes in the relative effect of policy variables at different lags would be desirable. A Cox proportionate hazard specification accommodates this easily but the underlying proportionality assumption is resoundingly rejected by the data.

²⁶ However, the standard errors are sizable so the estimates are statistically indistinguishable at conventional levels.

contributing to the estimation of policy effects across the two specifications are quite different and this makes some divergence in the point estimates less surprising.

The results in Table 9 consistently indicate that adding the protection of new products to an otherwise “Short” patent regime gives the greatest incremental boost to rapid market entry. For the specification with country fixed effects, shown in column one, we find also find a significant additional benefit from moving to a longer patent term. However, in no specification is there any evidence that having a drug patent extension affects the market entry of new pharmaceuticals within high-income countries.

All price regulation – whether moderate or extensive – tends to reduce the probability that a drug is launched in a high-income country within two years. There is a stronger effect found in the specification without country fixed effects, which may indicate an endogeneity problem. Companies might successfully push to relax price control in high-income countries that are perceived as more attractive in a way not well captured by the control variables. As for the poorer countries, the effect of moderate price regulation is again found to depend on the income level of a country. The estimates here indicate that moderate price control no longer lowers the probability of rapid entry once a country reaches a GDP per capita of about \$12,088, slightly below the median level for the group.

The first column of Table 10 contains estimation results for the “high quality” subset of NCE using the country fixed-effects specification. The overall probability of a high quality drug being launched within 2 years is over fifty percent higher than for an average NCE (33% vs. 20%). As for all drugs, short-term product patent protection encourages the launch of blockbusters. In contrast to all drugs, however, there is no incremental benefit from having the longest term of protection. Having any price control lowers the likelihood of entry and extensive price control is particularly problematic. The latter lowers the probability of rapid launch by 10.7 percentage points, or 33%.

The last results in Table 10 are within 2 and within 10 year estimates for the early (1982-92) period NCE. Because of the limited within-country variation in the policy variables during this shorter period, we use the random effects specification corresponding to column three in Table 9.

A high-income country increases the probability that new drugs are available to its consumers quickly by offering at least short-term protection to pharmaceutical products, as before, but for this early period there is an even larger incremental effect from moving to a longer term of protection (column 2). Some price control is weakly significant and extensive price control significantly diminishes the likelihood of rapid entry.

When considering whether drugs are “ever” launched in the high-income countries both patents and price regulation continue to have a role. In this longer time span, however, it is only long-term patent protection that is found to make a positive contribution. Recall from Figure 1 that later market entry implies a shorter effective patent life. Thus, the statutory term may need to be long if it is to create a period of exclusivity sufficient to allow a firm to cover the higher costs of entry into

high-income countries. It is somewhat surprising, then, to continue to find that offering a patent term extension has no discernible effect on eventual market entry nor on its timing. Finally, and again as we found for the poorer countries, extensive price control is far less damaging to the likelihood that a drug is ever launched than it is to the likelihood that it is launched quickly.

Maintaining an essential drugs list was found to have a significant dampening effect on market entry in the poorer countries in most specifications. We see the same negative effect within the high-income countries when considering all drugs, and of a similar relative magnitude. Having a national formulary is also associated with less rapid entry. Finally there is some evidence that the establishment of the European Medicines Evaluation Agency in 1995 as a centralized mechanism for obtaining marketing approvals within Europe has succeeded in speeding access to new drugs for consumers there. In specifications where the estimated effect of the EMEA is significant it is also large – increasing the probability of launch within 2 years by 25-30%.

Income Distribution and Demographic Characteristics

As one would expect, having a larger population and higher level of GDP per capita increases the likelihood that a country will have more drugs on the market and that they will become available quickly. In the estimations that include the Gini coefficient as a measure of income inequality, we find that the distribution of income is always also a significant determinant of market entry. The Gini coefficient, and its interaction with the log of GDP per capita, are statistically significant and show a pronounced pattern across the two income groups. As noted in the introduction, when an innovator firm considers launching products in one of the poorer countries, it may follow a strategy of setting low prices with small profit margins in an attempt to achieve extensive market penetration. Alternatively it may opt for higher prices with the expectation of reaching just the top of the market. We find that a lower-income country is more likely to get new drugs if it is unequal – ensuring that it has a wealthy “elite”. On the other hand, a high-income country is better off with a more equal distribution as this generates the largest “middle class”. Equality becomes less important as average income increases. These findings are consistent with the idea that there is a threshold level of income that makes an individual a potential consumer of new drugs. For countries with an average income below that threshold, inequality increases market size. For those above, inequality decreases market size – unless average income is so high that even when it is unequally distributed most consumers are above the threshold.

The age composition of a country’s population also appears as a very significant determinant of the speed and extent of drug launch. In the low- and middle-income countries, drugs are more likely to reach the market in countries with many children and those with a high proportion of elderly. In the high- income countries, having a larger proportion of children seems to be most important.

VII. Policy Simulations

This section considers the empirical implications of the econometric results discussed above. Table 11 gives the predicted probability that a drug arrives in a given country market within two years of its global launch. The predictions are for 1995 and the anti-infectives therapy class. They are based on the estimation of country fixed-effects models, using the high quality NCE for the high-income countries (Table 10, column 1) and the blockbuster sample for the low- and middle-income countries (unreported estimates). The columns on the left hand side indicate a range of different policy choices, while those on the right show how the predicted probabilities vary with these choices. The last row gives selected estimated standard errors – to give a sense of the precision of the predictions. Because the predictions are highly correlated across rows within a given column, and across columns within income groups, these should not be used to formally assess the statistical significance of differences. Bold typeface indicates changes that are significant.

The first three rows changes the patent regime, while the last three rows change price regulation. It is apparent from this table that a country's choices regarding intellectual property and price regulation can have a substantial impact on the likelihood that new pharmaceuticals are available to consumers quickly. In both lower- and high-income countries there appears to be scope to alter the probabilities by some 20-30% or more by virtue of these policy decisions.

Figures 4a and 4b present this finding in another form using the hazard model estimates presented in Table 8. These figures give predicted cumulative hazard rates for India. Each line represents the time path of market launches assuming different combinations of intellectual property and price control (PC) policies. As in Table 11, the predictions are for 1995 and the anti-infectives therapy class.

The pair of policies indicated in the top row under each figure has a change the patent term, while the pair in the second row has a change in the degree of price regulation. These changes generate similar-sized shifts in the cumulative hazard curves.

In each figure, the vertical axis indicates the predicted share of drugs launched in the given market by the lag indicated on the horizontal axis. Considering the upper dashed and dotted lines in Figure 4a that overlay each other, for example, we see that if India were to have some price control and also offer long (≥ 15 years) patent protection, a predicted 20% of all NCE would be marketed there within about five years of their global launch dates. Suppose that India then kept the longer term of patent protection but moved to more extensive price regulation (the lower solid line). One can ask the question: how many fewer drugs would arrive within five years with the new policy? Looking vertically at five years, the answer is that just 15% of all drugs – rather than the previous 20% - would be launched within this period as a result of the change in policy. One can also ask the question: with the new policy, how much longer would it take for 20% of all drugs to be launched? Looking

horizontally, the answer is that it would take some six and a half years – rather than five – as a result of the change in policy.

Irrespective of policy regime, ten years after global launch no more than 40% of all drugs are predicted to be on the Indian market (Figure 4a). In Figure 4b we see the far more comprehensive launch of blockbuster drugs, as well as greater scope for policy to have effect. At year six, for example, India is predicted to have more than fifty percent more new blockbuster pharmaceuticals on the market under a long process patent regime with moderate price control (dashed line) than if it were to offer long product patents and regulate the market extensively (solid line).

VII. Concluding Comments

Much attention has been paid to how price controls and the patent system determine pharmaceutical prices. We find that countries' choices about how to regulate pharmaceutical prices and protect innovation also have a significant influence on whether drugs become available to their consumers and how quickly. Short-term patent protection that includes products, or long protection only of manufacturing processes, are both patent regimes that tend to encourage more or faster launches in the developing world. Increasing the strength of a patent system to include long-term protection on pharmaceutical products appears to spur market entry – among the high-income countries. For the low- and middle-income countries that are currently being encouraged to move to stronger protection through trade policy, the evidence that extending protection enhances access to new pharmaceuticals is weak at best.

The standard argument regarding price regulation – that it will dissuade market entry – also seems to have more relevance among the high-income countries. For these countries, extensive price control is always found to lower the probability of market entry, and moderate regulation appears to do likewise, even in the long run. Not so for the poorer countries. There we find that although price regulation makes it less likely that new drugs will be available quickly, it does not appear to have a significant influence on whether new products are launched eventually.

As they stand these results are useful in tempering some of the arguments that can be made in international negotiations. Interpreting what they imply for public health and social welfare will require further analysis. If, for example, ten percent of NCE are no longer marketed in a country due to a policy change, this may be damaging or not depending on what was in that ten percent. Pharmaceuticals often have acceptable substitutes, and some “lifestyle” drugs may not be of great medicinal importance. Future research will explore the therapeutic significance of the pharmaceuticals that are launched slowly, or not at all, and the extent to which this failure is associated with there being substitutes available in the market.

A very poor country may also be quite willing to accept some delay in the arrival of innovative new pharmaceuticals as a result of regulation if it means that the drugs are priced within reach of more of the population when they finally reach the market. With cross-country data on product prices, this tradeoff could be assessed. Finally, giving innovators the strongest patent protection might be viewed as worthwhile irrespective of its effect on entry, on the grounds that it might boost R&D and the discovery of new NCE.

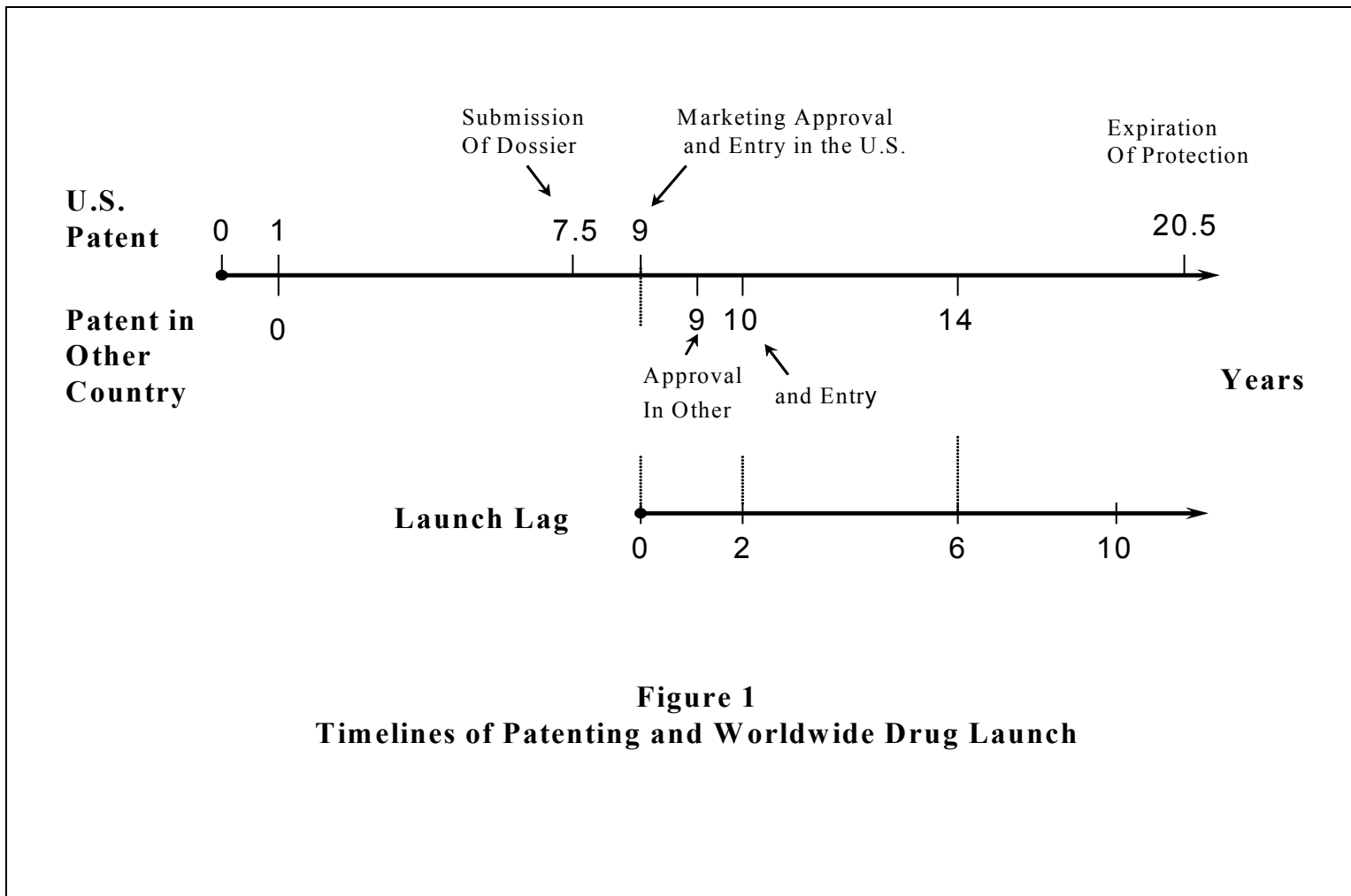


Table 1
NCE Global Launches per Year

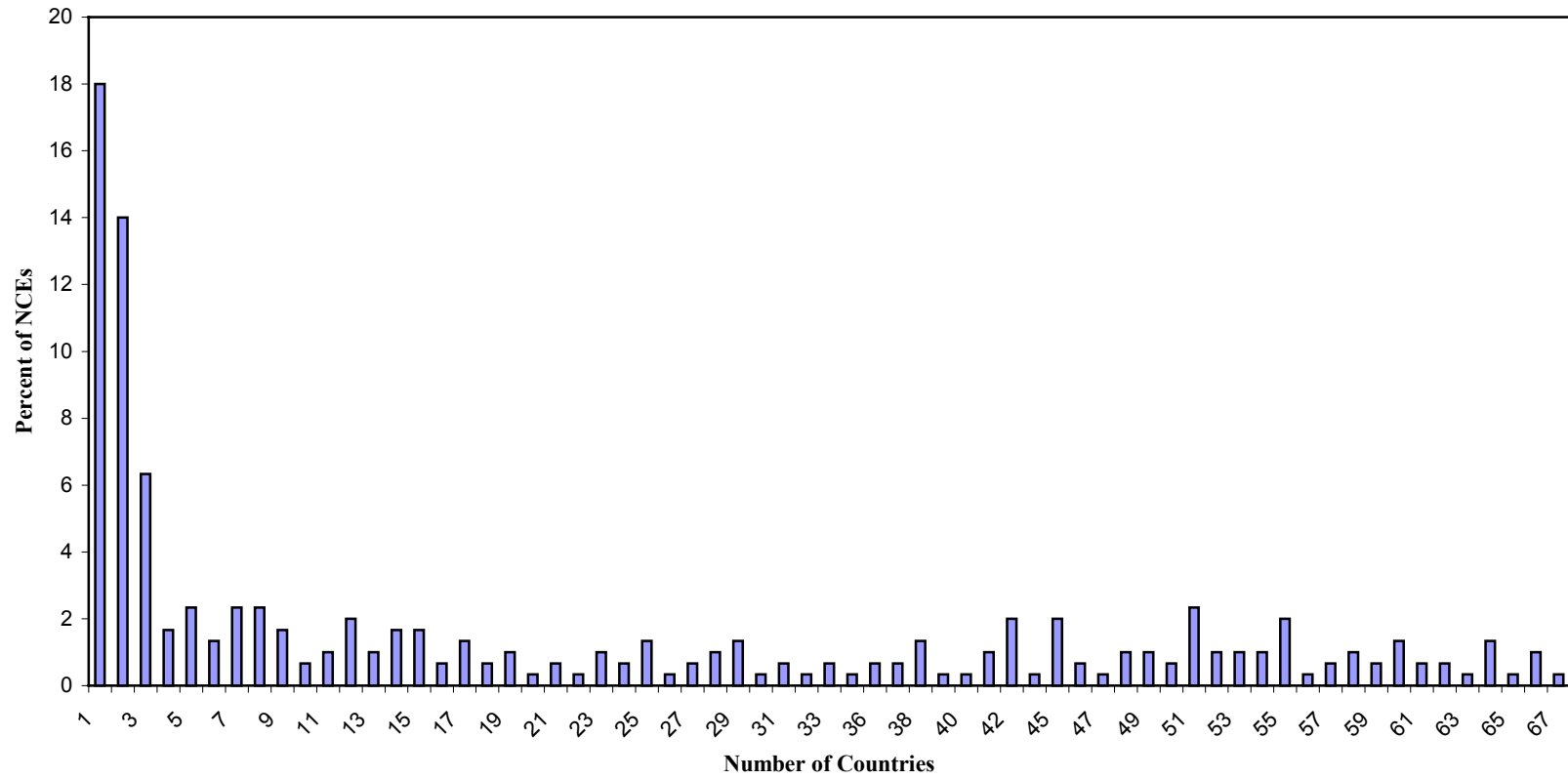
Year	Annual Block-busters	Total New Drugs
1982	11	36
1983	7	29
1984	5	34
1985	4	58
1986	7	45
1987	10	55
1988	10	43
1989	12	38
1990	13	42
1991	18	39
1992	9	43
1993	9	37
1994	9	41
1995	9	39
1996	18	42
1997	16	43
1998	11	39
1999	16	44
2000	7	35

Note: Blockbuster drugs are those launched in at least 4 countries of the E.U. and U.S. within two years for those with a global launch before 1995, and in at least 9 countries after that year.

Table 2			
Location of First Launch: Distribution Across Countries			
Country	No. First Launches	Years of Data	Pct. Of First Launches (Adjusted Share)
High Income Countries			
AUSTRALIA	3	21	0.28
AUSTRIA	12	21	1.28
BELGIUM	6	21	0.54
CANADA	10	21	1.02
DENMARK	18	21	1.82
FINLAND	12	21	1.19
FRANCE	44	21	4.38
GERMANY	74	21	7.36
GREECE	1	21	0.10
HONG KONG	1	21	0.09
IRELAND	15	21	1.53
ISRAEL	1	21	0.10
ITALY	61	21	6.08
JAPAN	231	21	23.99
NETHERLANDS	26	21	2.89
NEW ZEALAND	7	19	0.80
NORWAY	6	10	1.33
PORTUGAL	3	21	0.30
PUERTO RICO	16	9	3.68
SINGAPORE	6	19	0.70
SPAIN	23	21	2.38
SWEDEN	26	21	2.66
SWITZERLAND	36	21	3.67
UK	72	21	7.30
USA	163	21	16.95
Upper Income Countries			
ARGENTINA	7	21	0.72
BOLIVIA	1	11	0.24
BRAZIL	3	21	0.26
CHILE	1	21	0.10
CZECH REPUBLIC	1	10	0.20
MALAYSIA	5	21	0.53
MEXICO	16	21	1.66
POLAND	1	11	0.20
SOUTH AFRICA	6	21	0.65
SOUTH KOREA	1	15	0.11
TURKEY	1	21	0.09
VENEZUELA	6	21	0.58
Lower Income Countries			
COLOMBIA	1	21	0.07
DOMINICAN REPUBLIC	1	17	0.10
PERU	1	21	0.12
PHILIPPINES	4	21	0.45
RUSSIA	2	8	0.56
THAILAND	2	21	0.19
Low Income Countries			
BANGLADESH	1	10	0.19
FRENCH WEST AFRICA	2	11	0.40
PAKISTAN	1	21	0.08

Note: Total number of drugs launched = 836; launched 1995-2001 = 337.

Figure 2
Geographic Spread of New Drugs: Number of Countries Reached



Note: This figure includes the 300 drugs first launched 1/82 through 12/88.

Table 3
Launch Lags for NCEs that were First Marketed 1986-1992
(Months)

Country	# Drugs	Percentiles			Country	# Drugs	Percentiles		
		10 th	Median	90 th			10 th	Median	90 th
High Income					Upper Income				
AUSTRALIA	28	15	46.5	111	ARGENTINA	49	8	36	110
AUSTRIA	46	12	28.5	73	BRAZIL	43	22	52	131
BELGIUM	40	6.5	23	90.5	CHILE	39	13	41	104
CANADA	34	4	32.5	69	LEBANON	26	46	106	157
DENMARK	40	0.5	18	68	MALAYSIA	26	26	50.5	138
FINLAND	38	11	27.5	85	MEXICO	44	8	29	102
FRANCE	41	0	19	62	POLAND	6	34	43.5	98
GERMANY	54	0	18.5	45	SAUDI ARABIA	29	32	51	107
GREECE	44	13	37	120	SOUTH AFRICA	37	10	30	100
HONG KONG	37	13	27	88	SOUTH KOREA	53	24	49	110
IRELAND	38	0	22.5	88	TAIWAN	5	55	83	116
ISRAEL	29	28	52	102	TURKEY	40	23	55.5	95
ITALY	57	0	24	74	VENEZUELA	38	17	35.5	115
JAPAN	77	0	0	85	Lower Income				
NETHERLANDS	47	4	22	49	CENTRAL AMERICA	43	18	46	136
NEW ZEALAND	36	5	26.5	79	COLOMBIA	42	17	44.5	104
PORTUGAL	33	20	49	88	DOMINICAN				
SINGAPORE	33	18	45	109	REPUBLIC	35	25	49	111
SPAIN	37	18	30	111	ECUADOR	37	20	55	118
SWEDEN	46	0	17	86	EGYPT	30	37	73.5	133
SWITZERLAND	46	2	14	66	LATVIA	20	63	99.5	142
UK	50	0	16	51	MOROCCO	29	14	45	140
USA	46	0	20	69	PERU	36	24	57.5	159
					PHILIPPINES	49	6	35	98
					THAILAND	48	16	41.5	99

Table 3: Continued

Country	# Drugs	Percentiles		
		10 th	Median	90 th
Low Income				
FRENCH WEST AFRICA	10	19	47	131
INDIA	14	46	58	84
INDONESIA	42	22	43	97
PAKISTAN	38	23	57	118
(Unweighted) Means				
High Income	42.5	7.4	26.8	81.2
Upper Middle Income	33.5	24.5	50.9	114.1
Lower Middle Income	36.9	24.0	54.7	123.9
Low Income	26.0	27.5	51.3	107.5

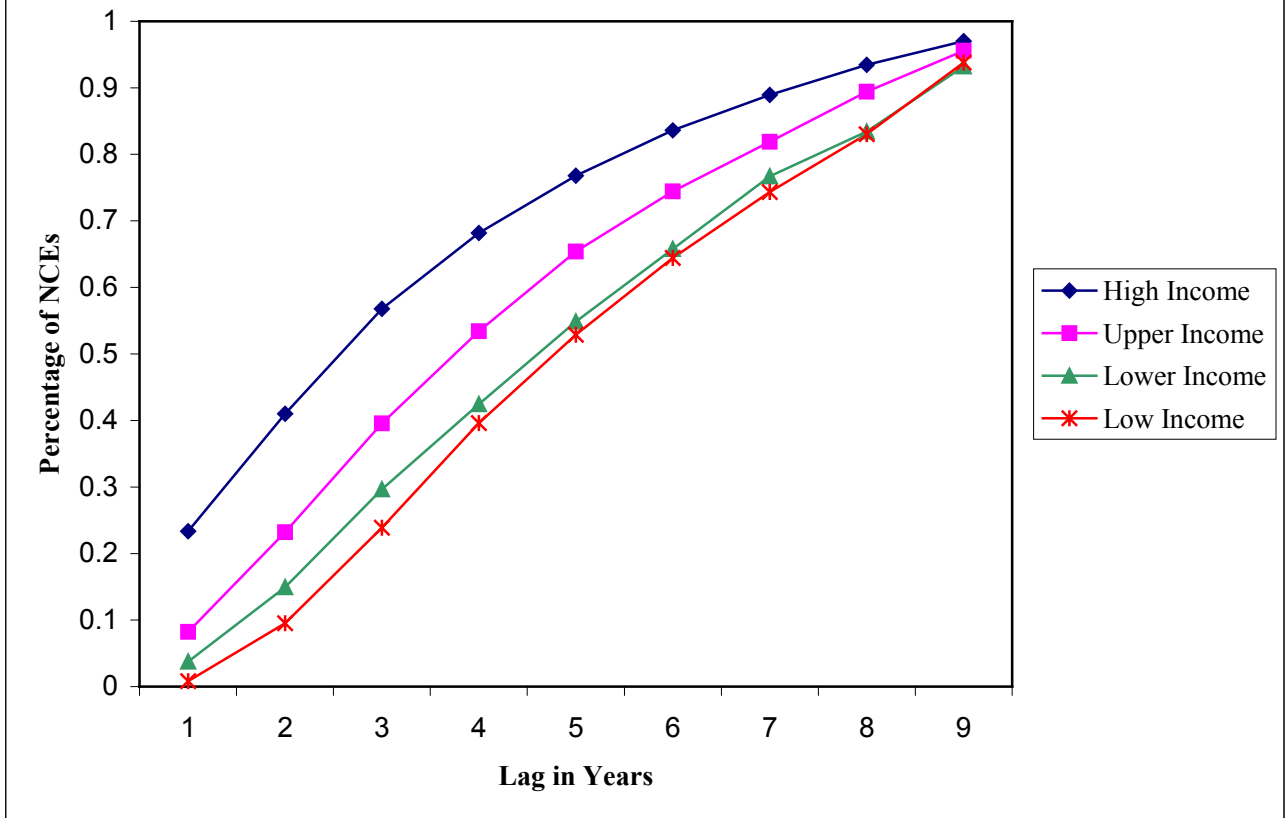
Notes: The sample includes the 122 NCE from the therapy classes A2B, C, J for which Indian data are available and, for a given country, only those NCE first marketed after the country entered the database.

**Table 4: The Arrival Speed of New Drugs
Percentage Marketed within Given Number of Years After Global Launch**

Percent Released	Upper Bound	Country	Years After First Launch								
			1	2	3	4	5	6	7	8	9
25%	28%	AUSTRALIA	5%	18%	39%	57%	68%	74%	83%	88%	95%
38	43	AUSTRIA	13	30	51	66	74	83	87	94	98
31	36	BELGIUM	19	40	61	72	79	85	91	94	98
30	35	CANADA	19	34	56	65	78	89	91	96	97
36	39	DENMARK	26	48	65	75	84	89	93	95	97
33	37	FINLAND	11	33	54	67	74	80	87	93	97
37	43	FRANCE	35	49	62	70	79	85	91	94	96
44	57	GERMANY	32	60	75	83	87	91	94	98	100
34	36	GREECE	6	23	41	56	69	78	85	91	94
29	33	HONG KONG	13	37	62	70	76	79	86	93	97
32	36	IRELAND	28	50	60	69	77	83	88	94	97
26	30	ISRAEL	3	17	27	52	69	74	83	93	98
49	54	ITALY	33	46	60	71	78	86	92	95	98
53	59	JAPAN	64	68	73	78	83	88	91	93	97
37	42	NETHERLANDS	31	53	68	79	84	90	92	94	98
28	30	NEW ZEALAND	20	41	53	65	72	81	86	91	94
29	34	PORTUGAL	11	23	40	47	65	76	84	91	97
26	26	SINGAPORE	14	35	53	66	76	82	89	95	98
36	40	SPAIN	12	28	48	61	70	78	85	92	96
34	37	SWEDEN	30	48	57	70	76	83	88	94	98
36	48	SWITZERLAND	35	56	70	79	83	87	90	92	96
40	45	UK	44	60	72	79	86	91	95	97	98
38	46	USA	34	48	62	71	78	89	93	94	98
42	47	ARGENTINA	13	27	44	60	70	76	80	84	93
32	36	BRAZIL	7	20	34	50	62	70	76	85	92
30	35	CHILE	7	25	43	53	65	74	83	91	95
22	24	MALAYSIA	13	33	56	76	83	88	91	94	99
35	38	MEXICO	14	33	47	60	73	81	87	93	98
23	26	SAUDI ARABIA	1	5	16	33	50	65	75	89	95
29	31	SOUTH AFRICA	15	35	53	63	69	77	84	91	98
31	34	TURKEY	1	10	24	35	52	64	76	88	96
26	28	VENEZUELA	4	21	38	50	64	75	84	90	94
31	35	CENTRAL AMERICA	3	19	35	46	63	72	81	88	95
31	35	COLOMBIA	6	15	30	47	59	67	79	85	97
27	30	ECUADOR	3	10	25	35	53	67	78	82	91
19	21	EGYPT	0	2	7	19	29	48	63	74	90
25	28	PERU	3	11	26	37	51	62	73	80	94
36	44	PHILIPPINES	8	25	44	58	67	74	83	86	93
34	35	THAILAND	5	23	41	55	63	71	80	88	93
26	28	INDONESIA	0	9	30	45	57	68	80	88	96
26	28	PAKISTAN	2	10	18	34	49	61	69	78	92

Notes: “Percent Released” is the share of global NCE launched in the row country within 10 years. “Upper Bound” assumes all observations with missing ingredient information are NCEs and grosses up the total launches accordingly.

Figure 3: Timing of Launch for NCEs Marketed within 10 Years



**Table 5: Low- and Middle-Income Countries
Probability of Launch within Two Years**

Policy Variables	With Country Fixed Effects		Without Country Fixed Effects			
	Marginal Effect	Estimated S.E.	Marginal Effect	Estimated S.E.	Marginal Effect	Estimated S.E.
Short process patent (< 15 years)	-0.010	0.011	-0.011	0.010	-0.003	0.011
Add long process (only) patents	0.034	0.015	0.033	0.016	0.022	0.013
Add short product patents (< 15 years)	0.010	0.015	0.021	0.014	0.012	0.012
Add long process & product patents	0.006	0.012	0.008	0.009	0.012	0.013
Drug patent extension					0.008	0.010
Some price control	-0.005	0.012	0.014	0.011	-0.155*	0.089*
Extensive price control	-0.028	0.010	-0.029	0.013	-0.036	0.009
Some price control * lnGDPcapita					0.021	0.011
Essential Drug List	-0.017	0.007	-0.017*	0.009*	-0.029	0.009
Standard Treatment Guidelines					0.036	0.011
National Formulary					0.017	0.007
Other Variables						
Health expenditure share Of GDP 1995/97			0.272	0.246	0.195	0.186
Private share of all health expenditure			0.041*	0.022*	0.038	0.017
LnPopulation	-0.257	0.120	0.024	0.005	0.018	0.005
LnGDPcapita	-0.063	0.020	0.109	0.028	0.111	0.023
Gini Coefficient			0.016	0.006	0.016	0.005
Gini*LnGDPcapita			-0.002	0.0007	-0.002	0.0006
Pct 65 yrs +	0.877	1.746	0.567	0.265	0.600	0.210
Pct 15-64 yrs	0.219	0.246	-0.279	0.119	-0.150*	0.096*
Population Growth			-0.401	0.430	-0.464	0.391
GDP Growth			0.022	0.056	0.035	0.055
Radios per capita 1990			-0.004	0.003	-0.009	0.002
Growth Radios 90-95			-0.004	0.005	-0.017	0.005
Doctors/1000 in 1990			0.011	0.005	0.007*	0.004*
Growth Doctors 90-95			-0.0007	0.002	-0.002	0.002
No. Obs./ Observed P Pseudo R²		19901/0.089		17917/0.091		17917/0.091
		0.155		0.132		0.136

Notes: All specifications control for year of first launch and therapy class. Huber-White robust estimated standard errors allow for heteroscedasticity; and intra-country correlation in the disturbances in specifications without country fixed effects. Bold typeface and * indicate coefficients significant at $\alpha = 0.05$ and 0.10 , respectively. Marginal effects estimated at variables means (all data) and for a discrete change in the case of dummy variables. As a result of missing inequality information, Lebanon, Puerto Rico, Saudi Arabia and Taiwan are dropped in estimations without country FE.

Table 6
Low- and Middle-Income Countries
Probability of Launch within Two Years

Policy Variables	All Drugs		LDC Concentrated		“Blockbusters”	
	Marginal Effect	Estimated S.E.	Marginal Effect	Estimated S.E.	Marginal Effect	Estimated S.E.
Short process patent (< 15 years)	-0.003	0.011	0.004	0.019	-0.003	0.037
Add long process (only) patents	0.021*	0.013*	0.041	0.024	0.033	0.040
Add short product patents (< 15 years)	0.003	0.015	0.002	0.021	0.051	0.042
Add short * strong	0.053*	0.030*				
Add long process & product patents	0.018	0.014	0.024*	0.014*	0.001	0.033
Add long * strong	-0.045	0.031				
Drug patent extension	0.011	0.011	0.057	0.017	0.008	0.035
Some price control	-0.172	0.092	-0.265	0.121	-0.539	0.190
Extensive price control	-0.034	0.010	-0.047	0.018	-0.122	0.034
Some price control * lnGDPcapita	0.023	0.011	0.033	0.013	0.080	0.032
Essential Drug List	-0.029	0.009	-0.038	0.015	-0.110	0.027
Standard Treatment Guidelines	0.035	0.011	0.074	0.019	0.134	0.037
National Formulary	0.015	0.008	0.023	0.009	0.065	0.027
No. Obs./ Observed P	17917/0.091		4499/0.110		4865/0.249	
Pseudo R ²	0.136		0.181		0.198	

Notes: See notes to Table 5. All specifications control for year of first launch and therapy class. “LDC Concentrated” includes only NCE from the therapy classes A (Alimentary tract and metabolism) and J (Systemic anti-infectives). Blockbuster drugs are those launched in at least 4 countries of the E.U. and U.S. within two years for those with a global launch before 1995, and in at least 9 countries after that year.

Table 7
Low- and Middle-Income Countries
Probability of Launch within Two and Ten Years

Policy Variables	All Drugs				"Blockbusters"			
	Within 2		Within 10		Within 2		Within 10	
	Marginal Effect	Estimated S.E.	Marginal Effect	Estimated S.E.	Marginal Effect	Estimated S.E.	Marginal Effect	Estimated S.E.
Short process patent (< 15 years)	-0.016*	0.009*	-0.057	0.016	0.012	0.037	-0.064	0.057
Add long process (only) patents	0.086	0.022	0.047*	0.029*	0.171	0.057	-0.0002	0.070
Add short product patents (< 15 years)	0.005	0.008	0.057	0.021	0.042	0.032	0.152	0.071
Add long process & product patents	0.029	0.015	0.016	0.034	-0.008	0.044	-0.085	0.102
Drug patent extension	-0.001	0.010	0.035	0.029	0.027	0.041	0.024	0.043
Some price control	0.012	0.110	0.052	0.213	0.258	0.485	0.210	0.465
Extensive price control	-0.025	0.008	-0.007	0.017	-0.124	0.037	-0.084	0.063
Some price control * lnGDPcapita	-0.001	0.013	0.012	0.028	-0.033	0.048	-0.024	0.071
Essential Drug List Standard Treatment Guidelines	-0.023	0.016	-0.077	0.027	-0.067	0.043	-0.151	0.044
National Formulary	0.012	0.013	0.070	0.022	0.071	0.036	0.104	0.052
No. Obs./Observed P	0.042	0.010	0.016	0.025	0.158	0.037	0.088	0.055
Pseudo R ²	8967/0.059 0.076		8831/0.302 0.046		2126/0.185 0.131		2076/0.680 0.108	

Notes: See notes to Tables 5 and 6. These estimations include only NCE first launched in 1992 or earlier.

**Table 8: Hazard Estimations
Low- and Middle-Income Countries**

Policy Variables	All Data		“Blockbusters”	
	Coefficient	Estimated S.E.	Coefficient	Estimated S.E.
Short process patent (< 15 years)	0.068	0.102	0.149	0.110
Add long process (only) patents	-0.224	0.102	-0.259	0.110
Add short product patents (< 15 years)	-0.238	0.121	-0.228*	0.130*
Add long process & product patents	0.047	0.095	0.094	0.102
Drug patent extension	0.002	0.094	-0.072	0.101
Some price control	0.133	0.103	0.146	0.108
Extensive price control	0.349	0.094	0.442	0.103
Essential Drug List	0.110*	0.060*	0.066	0.065
Standard Treatment Guidelines	0.027	0.069	0.128*	0.076*
Control Variables				
LnPopulation	3.451	1.020	3.403	1.094
LnConsumption	0.537	0.177	0.521	0.186
Pct 65 yrs +	21.953*	13.208*	19.044	14.128
Pct 15-64 yrs	-6.292	1.988	-8.261	2.158
γ	0.554	0.012	0.485	0.011
θ	3.302	0.159	0.569	0.056
No. Observations.		21187		6538
Log likelihood		-18041.3		-6780.9

Notes: See notes to Table 5. Blockbuster drugs are those launched in at least 4 countries of the E.U. and U.S. within two years for those with a global launch before 1995, and in at least 9 countries after that year. Both specifications use a log-logistic hazard function with a gamma distributed multiplicative factor to capture unobserved heterogeneity. They include country, year, and therapy class fixed effects.

Table 9
High-Income Countries
Probability of Launch within Two Years

Policy Variables	With Country Fixed Effects		Without Country Fixed Effects			
	Marginal Effect	Estimated S.E.	Marginal Effect	Estimated S.E.	Marginal Effect	Estimated S.E.
Short product patents (< 20 years)	0.091	0.013	0.050	0.020	0.057	0.020
Add long process and/or product patents	0.031	0.013	0.064	0.039	0.059	0.045
Drug patent extension					0.006	0.021
Some price control	-0.038	0.014	-0.053	0.024	-0.667	0.243
Extensive price control	-0.058	0.020	-0.127	0.025	-0.124	0.026
Some price control * lnGDPcapita					0.071*	0.036*
Essential Drug List	-0.025	0.019	-0.068	0.017	-0.084	0.033
Standard Treatment Guidelines					0.029	0.086
National Formulary					-0.039	0.026
EMEA	0.034	0.017	0.026	0.042	0.041	0.043
Other Variables						
Health expenditure share Of GDP 1995/97			-2.602	1.012	-2.393	1.038
Private share of all health expenditure			0.205	0.178	0.184	0.179
LnPopulation	0.436	0.129	0.041	0.006	0.043	0.006
LnGDPcapita	-0.154	0.056	-0.673	0.346	-0.766	0.359
Gini Coefficient			-0.256	0.111	-0.273	0.116
Gini*LnGDPcapita			0.025	0.011	0.027	0.011
Pct 65 yrs +	-3.519	0.470	-0.617	0.572	-0.534	0.628
Pct 15-64 yrs	-0.544	0.382	-1.610	0.435	-2.097	0.477
Population Growth			-1.781*	0.987*	-1.811	0.932
GDP Growth			0.265	0.364	0.282	0.336
Doctors/1000 in 1990			-0.008	0.015	-0.012	0.016
Growth Doctors 90-95			-0.052	0.044	-0.047	0.044
No. Obs./ Observed P	18889/0.205		15383/0.225		15383/0.225	
Pseudo R ²	0.104		0.090		0.091	

Notes: See notes to Table 5. As a result of missing inequality information, Kuwait, New Zealand, Singapore and UAE are dropped from the estimations without country FE.

Table 10
High-Income Countries
Probability of Launch

Policy Variables	“High Quality Drugs”		All Drugs			
	With Country FE		Within 2		Within 10	
	Marginal Effect	Estimated S.E.	Marginal Effect	Estimated S.E.	Marginal Effect	Estimated S.E.
Short product patents (< 20 years)	0.188	0.025	0.042	0.013	-0.011	0.014
Add long process and/or product patents	0.035	0.028	0.087	0.022	0.053	0.021
Drug patent extension			-0.013	0.020	0.025	0.021
Some price control	-0.056	0.029	-0.379*	0.172*	-0.638	0.128
Extensive price control	-0.107	0.040	-0.095	0.017	-0.055*	0.029*
Some price control * lnGDPcapita			0.041*	0.023*	0.077	0.024
Essential Drug List	0.005	0.039	-0.057	0.023	-0.089	0.019
National Formulary			-0.022	0.018	-0.010	0.028
EMEA	0.088	0.031				
No. Obs./ Observed P	7951/0.335		9258/0.166		9258/0.371	
Pseudo R ²	0.113		0.058		0.030	

Notes: See notes to Tables 5. “High Quality” is the subset of NCE that are marketed in either the U.S. or the U.K. within 2 years of first global launch. The U.S. and U.K. are not included in these estimations. Results for “All Drugs” are based only on NCE first launched in 1992 or earlier and do not include country fixed effects.

Table 11
Predicted Probability of Launch within Two Years
“Blockbuster” or “High Quality” Drugs

Policy Scenario				Country				
Product Patent	“Long” Patent Term	Any Price Control	Extensive Price Control	Brazil	Egypt	Thailand	France	Canada
No	No	Yes	No	0.661	0.217	0.386	0.272	0.343
No	Yes	Yes	No	0.777	0.332	0.584		
Yes	Yes	Yes	No	0.801	0.363	0.556	0.545	0.642
Yes	Yes	No	No	0.809	0.374	0.568	0.607	0.683
Yes	Yes	Yes	Yes	0.666	0.221	0.391	0.422	0.503
S.E. on final prediction				0.096	0.098	0.097	\	0.050

Note: All scenarios assume that at least short process patents are available. “High Quality” (high-income group) and “Blockbuster” (low-and middle-income group) are defined in notes to Tables 6 and 10. The predictions given are based on a model with country fixed effects and use time-variant country characteristics for 1995, and the anti-infectives therapy class. A “long” statutory term is > 14 years for Brazil, Egypt, and Thailand; > 19 years for France and Canada. Bold typeface indicates comparisons that likely represent statistically significant differences.

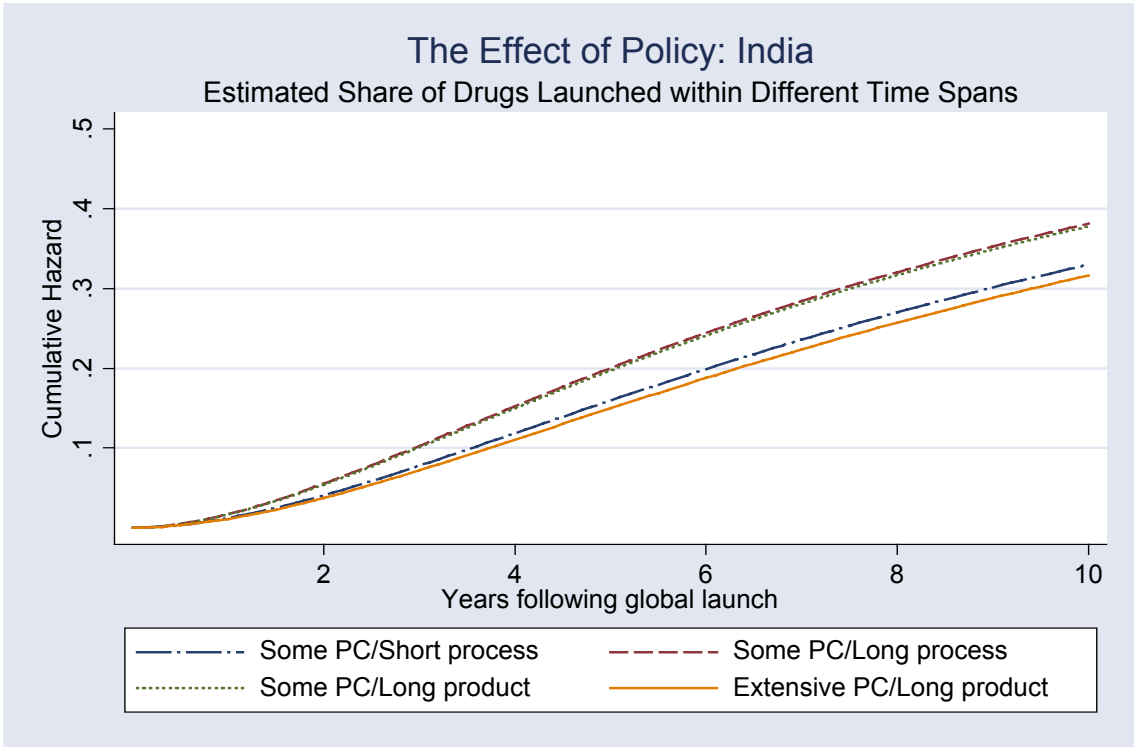


Figure 4a

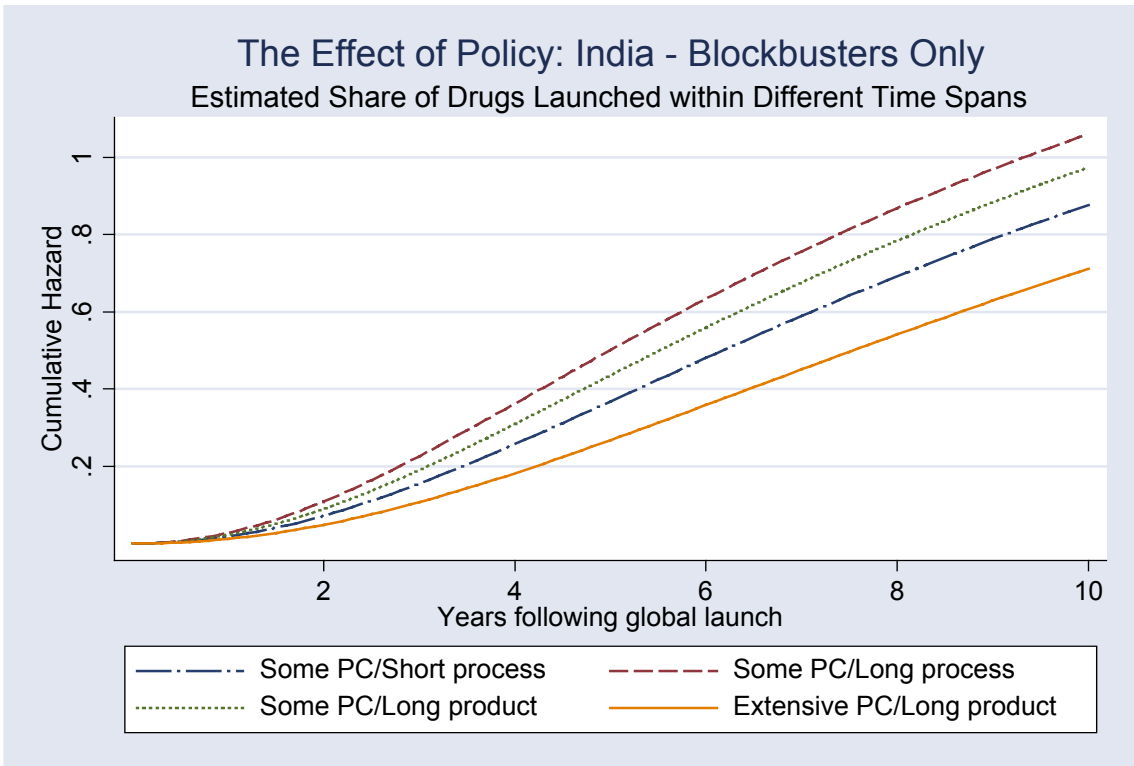


Figure 4b

**Table A1
Launch Path for Ciprofloxacin**

Launch Within 2		Lag
PHILIPPINES	10/1986	0
GERMANY	2/1987	4
UK	2/1987	4
CENTRAL AMERICA	9/1987	11
FINLAND	9/1987	11
AUSTRIA	9/1987	11
USA	11/1987	13
SWITZERLAND	11/1987	13
CHILE	12/1987	14
MEXICO	12/1987	14
AUSTRALIA	1/1988	15
SWEDEN	2/1988	16
NEW ZEALAND	3/1988	17
DENMARK	4/1988	18
JAPAN	7/1988	21
INDONESIA	8/1988	22
SPAIN	8/1988	22
THAILAND	8/1988	22
NETHERLANDS	9/1988	23
PERU	10/1988	24
Launch Within 10		
HONG KONG	11/1988	25
GREECE	12/1988	26
CANADA	1/1989	27
ISRAEL	2/1989	28
IRELAND	4/1989	30
ARGENTINA	4/1989	30
ITALY	5/1989	31
COLOMBIA	5/1989	31
ECUADOR	6/1989	32
TURKEY	6/1989	32
PORTUGAL	8/1989	34
BRAZIL	9/1989	35
VENEZUELA	9/1989	35
FRANCE	2/1990	40
MALAYSIA	3/1990	41
BELGIUM	3/1990	41
SOUTH AFRICA	6/1990	44
INDIA	8/1990	46
PAKISTAN	3/1991	53
SAUDI ARABIA	12/1991	62
SINGAPORE	7/1993	81
EGYPT	10/1994	96

Table A2: Variable Definitions	
Short process patent (< 15 years)	Dummy = 1 if country protection only on pharmaceutical processes. When the statutory term is defined to end “X years after grant,” the granting process is assumed to take 2 years. As is appropriate for some countries, we take the min or max of “years from grant” and “years from filing” to estimate the statutory term.
Short product patents (< N years)	Dummy = 1 if product patents are offered.
Long process (only) patents	Dummy = 1 if country offers only process patents with a statutory term ≥ 15 years.
Long process & product patents	Dummy = 1 if both product and process innovations covered and term is at least 15 years.
Long process and/or product patents	Dummy = 1 if either process or both process and product protection is offered and the term is at least 20 years.
Strong	“Strong” is a variable that takes on values between 0 and 1, with a higher value indicating that a country has more limits on how patent rights can be curtailed.
Drug Patent Extension	Dummy = 1 if firms may apply for an extension of the statutory term of patent protection to compensate for time taken in the marketing approvals process.
Some Price Control	Dummy = 1 if country has a formal price control mechanism but it is not extensive.
Extensive Price Control	Dummy = 1 if price control covers most of the market and/or is viewed as particularly restrictive.
Essential Drug List	Dummy =1 for national adoption of an EDL
Standard Treatment Guidelines	Dummy = 1 for national adoption of standard treatment guidelines
National Formulary	Dummy = 1 for having a national formulary
EMEA	Dummy = 1 for years when a country is a member of the European Medicines Evaluation Agency
Health Expenditure Share of GDP 1995/97	Mean annual total health expenditure during the years 1995-97 in 1995 U.S. \$
Private Share of All Health Expenditure	Mean private health expenditure for 1995-97 as a share of mean total health expenditure 1995-97
LnPopulation	Log of population
LnGDPcapita	Log of GDP per capita in 1995 U.S. \$
Gini Coefficient	Estimated Gini coefficient of inequality (of household per-capita income in most cases) taken as close as possible to early 1990 but ranging from years 1987-99.
Pct 65 yrs +	Percentage of total population aged 65 and older
Pct 15-64 yrs	Percentage of total population aged 15 through 64
Population Growth	Pct. Growth in total population over previous year
GDP Growth	Pct. Growth in GDP over previous year
Radios per capita 1990	Average radios per person in 1990
Growth Radio 90-95	Percent increase in radios per 100 between 1990 and 1995
Doctors/1000 in 1990	Doctors per thousand people as of 1990/2 (1990 if available)
Growth Doctors 90-95	Percent increase in doctors per thousand between 1990/2 and 1995/7 (1990 and 1995 if available)

Table A3: Variable Distributions

	All Data				Early Period (1982-93)			
	Low/Middle Income		High Income		Low/Middle Income		High Income	
	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
Policy Variables								
Process patent	0.853	0.345			0.752	0.422		
Short product patents (< N years)	0.536	0.492	0.880	0.326	0.334	0.463	0.837	0.370
Long process (only) patents	0.614	0.487			0.407	0.492		
Long process & product patents	0.473	0.499			0.263	0.441		
Long process and/or product patents			0.779	0.415			0.693	0.461
Drug patent extension	0.614	0.487	0.856	0.352	0.407	0.492	0.819	0.386
Some price control	0.833	0.372	0.784	0.412	0.319	0.466	0.347	0.476
Extensive price control	0.397	0.489	0.349	0.477	0.462	0.499	0.379	0.485
Essential Drug List	0.415	0.490	0.921	0.270	0.131	0.335	0.884	0.321
Standard Treatment Guidelines	0.178	0.373	0.972	0.164	0.082	0.272	0.957	0.204
National Formulary EMEA Member	0.173	0.371	0.755	0.430	0.070	0.252	0.623	0.485
			0.177	0.382				
Control Variables								
LnPopulation	17.205	1.255	16.398	1.317	17.384	1.158	16.518	1.241
LnGDPcapita	7.661	0.840	9.950	0.407	7.570	0.840	9.875	0.394
LnPop*LnGDPcapita	131.49	13.74	163.31	15.74	131.20	13.22	163.23	15.23
Gini Coefficient	43.677	10.235	32.453	6.188	45.530	9.402	32.710	6.217
Gini*LnGDPcapita	334.43	95.99	322.84	58.41	345.98	95.07	322.79	57.66
Pct 65 yrs +	0.053	0.031	0.128	0.033	0.043	0.017	0.125	0.027
Pct 15-64 yrs	0.600	0.005	0.666	0.027	0.582	0.035	0.665	0.028
Population Growth	0.018	0.010	0.008	0.012	0.021	0.009	0.007	0.010
GDP Growth	0.015	0.053	0.022	0.026	0.0109	0.0648	0.020	0.025
Radios per capita 1990	0.331	0.203	0.824	0.385	0.301	0.180	0.848	0.386
Growth Radios 90-95	0.136	0.425	0.139	0.934	0.157	0.474	0.039	0.067
Doctors/1000 in 1990	1.343	1.037	2.432	1.063	1.345	1.018	2.474	1.077
Growth Doctors 90-95	0.601	1.842	0.158	0.273	0.469	1.448	0.154	0.279
Health Expenditure Share of GDP 1995/97	0.054	0.019	0.080	0.019	0.053	0.019	0.081	0.018
Private Share of All Health Expenditure	0.531	0.170	0.309	0.146	0.551	0.152	0.311	0.127

**Table A4: Changes in Price Control and Patent Protection
Early Period (1982-92) and Late Period (1993-2000)**

	Any Price Control		Extensive Control		Process Patents		Product Patents		Statutory Term	
	Early	Late	Early	Late	Early	Late	Early	Late	Early	Late
ARGENTINA			0						+	+
BANGLADESH	+		+	0						
BOLIVIA										+
BRAZIL				0		+		+		
BULGARIA				0						
CENTRAL AMERICA	+	0	+	0	+		+	+		
CHILE					+		+			
COLOMBIA			0				+		+	+
CZECH REPUBLIC			0							
DOMINICAN REPUBLIC			0							
ECUADOR									+	+
EGYPT										
FRENCH WEST AFRICA			0							
HUNGARY			0					+		+
INDIA				0						
INDONESIA	+				+		+			
JORDAN								+		+
LATVIA	0	+	0							
LEBANON								+		+
MALAYSIA									0	
MEXICO	+		+	0	+		+			
MOROCCO								+		
PAKISTAN								+		+
PARAGUAY										
PERU			0				+		+	+
PHILIPPINES	+									+
POLAND			0					+		+
PUERTO RICO										+
RUSSIA	0	+	0							
SAUDI ARABIA					+		+			
SLOVAK REPUBLIC	0	+	0							
SOUTH AFRICA		+		+						
SOUTH KOREA				0						
TAIWAN	+									+
THAILAND							+		+	
TUNISIA										
TURKEY						+				
URUGUAY								+		+
VENEZUELA								+	+	+

	Any Price Control		Extensive Control		Process Patents		Product Patents		Statutory Term	
	Early	Late	Early	Late	Early	Late	Early	Late	Early	Late
AUSTRALIA										+
AUSTRIA							+			
BELGIUM									+	
CANADA	+									
DENMARK	+		+, 0				+			
FINLAND				+				+		
FRANCE										
GERMANY	+	0								
GREECE										
HONG KONG									+	
IRELAND										
ISRAEL										
ITALY				0						
JAPAN										+
KUWAIT	+		+							
LUXEMBOURG										
NETHERLANDS		+								
NEW ZEALAND	+									+
NORWAY				+			+			
PORTUGAL	+							+		+
SINGAPORE										
SLOVENIA	0	+	0	+						
SPAIN							+			
SWEDEN				0						
SWITZERLAND										
UK										
UNITED ARAB EMIRATES										
USA										+

Note: Changes are only indicated for a country during periods for which launch information is also available.
+ indicates an increase and 0 a decrease in the variable.

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