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Impact of Patents on Access to HIV/AIDS Drugs in Developing Countries

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September 19, 2003

* This is a revised version of working paper No. 92 of the Center for International Development at Harvard University. We thank Victor Aguirregabiria, Richard Caves, Ian Cockburn, Markus Mobious, Ariel Pakes, Dani Rodrik, Albert Saiz, George Symeonidis and Elena Zoido for helpful comments and suggestions. We gratefully acknowledge the comments from many participants at Harvard and NBER Seminars,and the EARIE 2003 Conference. While working on this paper Watal was Visiting Fellow at the Center for International Development (CID) at Harvard University and Borrell was Post-doctoral Fellow at Harvard Economics Department. We thank our respective hosts. We gratefully acknowledge funding from the CID. Borrell gratefully acknowledges unrestricted educational grants from Fundacion Ramon Areces (Madrid, Spain) and The Merck Foundation, the philanthropic arm of Merck & Co. Inc., Whitehouse Station (New Jersey, USA). Research assistance from Friederike Hesse (Kennedy School of Government) and Jimmy Liu (Harvard College) is also gratefully acknowledged. The opinions stated are only those of the authors, and any error or omission remains only under the authors' responsibility. In particular the views expressed in this paper do not engage the responsibility of the WTO Secretariat nor of WTO Members, individually or collectively, and does not present authoritative interpretations of WTO provisions, which can only be done by WTO Members jointly. E-mails: Jayashreewatal@hotmail.com, jrborrell@ub.edu

Abstract

This paper uses sales data on HIV/AIDS drugs in developing countries to assess empirically whether patents expand or reduce new drugs sales. There can be two possible effects of patents on sales of new drugs. On the one hand, patents might lead to higher prices and lower sales due to the lack of competition from imitators in the market place. On the other hand, patents might expand (or reduce) sales of drugs because patents give the owners of the innovation incentives to distribute it quicker (or slower). It is an empirical question to assess whether these two arguments have opposing effects, and if so which one dominates. Our main finding is that on average patents increase availability of new drugs (from 28% to 33%), but patents reduce sales by 59% once the drug is available in the market place. The net effect of these two counterbalancing effects is that patents reduce sales by 34%. This is a significant impact, but it cannot be blamed for the overwhelming lack of access to HIV/AIDS therapy in developing countries: switching all drugs under patent regime to a no patent regime in our sample countries would have only increased the percentage of AIDS patients with access to new drugs from 0.88% to 1.18% between 1995 and 1999.

Keywords: Patents; Entry; Pricing; Access; Pharmaceuticals.

JEL Codes: L65; K11; O34.

1 Introduction

Millions of patients living with the human immunodeficiency virus (HIV) in low and middle income countries lack access to effective and safe drugs that change the late stage of that infection, the Acquired Immune Deficiency Syndrome (AIDS) from a death sentence to a chronic disease. Those drugs are called anti-retro-viral drugs (ARV). Patent rights are at the center of the public debate on access to new drugs. Patents allegedly impede the access of a vast majority of patients in poor countries to new drugs. However, this statement has not been assessed empirically. This paper tackles the question of whether patents reduce new drug sales in low and middle-income countries.

Some papers estimate the impact of patents on drug markets. Most study the effect of patent expiration on drug pricing and shares in the US like the papers by the following authors: Hurwitz and Caves (1988); Caves, Whinston and Hurwitz (1991); Grabowski and Vernon (1992); Frank and Salkever (1992, 1997); Griliches and Cockburn (1994); Hellerstein (1994); and, Fisher and Griliches (1995). Hudson (1992 and 2000) analyzes drug pricing

dynamics and patent expiration not only in the US, but also in the UK, Germany, France, and Japan.

On the other hand, very little attention has been devoted to studying the impact of patent rights on drug introduction, pricing, and sales in developing countries. Some papers attempt to simulate the likely effects of product patents on average drug prices: Challu (1991), Fink (2000), Watal (2000), Maskus and Eby-Konan (1994), and Subramanian (1995). Lanjouw (1998) discusses more generally the socio-economic effects of the introduction of patents in India, and Lanjouw and Cockburn (2001) study empirically the positive impact of patent protection on research on drugs that address the needs of patients in poor countries (a point raised formally by Diwan and Rodrik, 1991).

This paper tries to fill the gap in the empirical literature on drug markets. It investigates the impact of patents on unsubsidized sales of new ARV drugs in a sample of low and middle-income countries in the late 1990s.

We hypothesize that the existence of patent regimes has two possible effects on sales to drugs in low and middle-income countries. On the one hand, the expectation of patent availability may increase prices and reduce sales due to smaller competitive pressures (lack of competition from imitators in the market place). Patents legally prevent unauthorized manufacture, sale or offering for sale, importation and use of the patented product during the patent term. This prevents competition between the innovator of the drug (or any of its licensees) and unauthorized providers of products that contain the same therapeutically active substance or of products that only differ trivially from these. The lack of close competitors - usually local firms competing with the global and innovative firms - is expected to shift prices up and decrease demand in market equilibrium.

On the other hand, the expectation of patent availability might expand (or reduce) sales of drugs. Patents might expand sales of drugs in developing countries because patent owners may have an incentive to distribute them quicker across countries. Market exclusivity usually means higher prices and greater income flows which, in turn, may encourage patent holders to launch new drugs in low and middle income countries soon after they are

launched in high income countries.[1] Imitators usually require some time after a drug is launched for the first time by the innovator to produce that drug in countries where patent rights are not granted. This is because imitators do not have detailed information on the characteristics of the new drug until the content of the patent is disclosed through publication of the patent application and more importantly after the product is available in any market around the world.[2] Without the innovator's technical assistance, imitators usually lack the expertise to produce the new drug immediately after it has been marketed for the first time. The actual time lag between the worldwide launch of a product by the innovator and the fastest imitator depends on several factors, including the technological complexity of the product and the skills of the domestic pharmaceutical industry.

Alternatively, patents may reduce sales of drugs because patents may give the owners of the invention incentive to distribute them slower across countries. Exclusivity has a price in terms of patenting fees and legal enforcement expenses. Additionally, firms maximizing worldwide profits of breakthrough drugs (drugs that enter in the market at high prices that decay gradually though time) may be tempted to launch new drugs in some low- price countries later or not at all in order to avoid the risk of parallel traders undercutting their profit flows from their products in high-price countries. Patents allow innovative drug firms to delay entry in a market without the risk of being surpassed by the entry of an imitator who could eventually become the first in marketing the new drug. There is evidence that suggests that being the first to introduce the product is important in markets of experience goods such as pharmaceuticals regardless the patent regime (see McRae and Tapon, 1985; Gorecki, 1986 and 1987; Caves, Whinston and Hurwitz, 1991; Grabowski and Vernon, 1992; and Hollis, 2002). But, patent rights may reduce the competitive pressure to launch new drugs quickly across countries after new drugs are launched in high price countries.

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[1] Lanjouw and Cockburn (2001) report that interviewed drug firm executives believed that 'faster introductions of new products and greater investments in marketing and educating the local medical community about new therapies' were the major benefits from the introduction of product patents in developing countries.

[2] Most countries, other than the United States, provide for publication of patent applications 18 months from the date of their filing. The American Inventor's Protection Act of 1999 required for the first time in the US publication of all non-provisional patent applications filed after November 29, 2000. It also allowed publication of earlier-filed pending applications on request. However, the TRIPS Agreement does not require that Patent Offices provide for such publication prior to patent grant.

It is an empirical question to assess whether the effect of patents on sales and on introduction in the market have opposing effects, and if so which one dominates. It depends largely on how much patents constrain competition and shift prices up and demand down in market equilibrium, and on how intensively patent enforcement speed up or slow down the introduction of new drugs across markets. This paper uses sales data on HIV/AIDS drugs in a sample of 34 low and middle income countries between 1995 and 1999. It estimates a sample selection model to assess empirically the impact of market exclusivity on sales. It is pertinent to note that this period did not see any significant discounts on the prices of patented drugs, which came mostly after 2000.

Our main finding is that the patents have a negative effect on unsubsidized sales of HIV/AIDS drugs in the countries of our sample. Switching all drugs from a patent regime to no-patent regime would have actually increased the percentage of AIDS patients that are treated using new drugs by 34%. However, such increase only shifts market coverage up from 0.88% to 1.18%. Thus, even with such a patent regime change, 98.92% of AIDS patients would have been excluded from new drug therapy.

The plan of the paper is the following: in section 2 (data and method), we describe how we measure the effect of patents on drug sales, and the characteristics of the data set. In section 3 (results), we estimate the impact of patents on access to ARV therapy and we obtain some in-sample predictions of market coverage in different patent regimes. Finally, we conclude in section 4.

2 Method and Data

2.1 Method

We estimate two key simultaneous relationships to tackle the question under study: (1) the relationship between the likely entry decision across drug-country-year triplets and patents; and (2) the relationship between market coverage (i.e. mean coverage of patients under annual treatment with a specific ARV drug) and patents conditional on drug entry decisions and patent regime. Our key identification assumption is that patent regime is exogenously set by the government regardless entry decisions by drug innovators and imitators.

Let a^{i}_{jt} be a binary indicator that equals one when any drug *j* is available in any country *i* at any given observed year *t*, and zero otherwise. The unconditional expected share of AIDS patients that had access to any drug, $E(s^{i}_{jt})$, is equal to the probability of having that drug locally available ($a^{i}_{jt}=1$) times the expected share of patients that access to the drug conditional on having the drug available locally, $E(s^{i}_{jt} | a^{i}_{jt}=1)$ as shown below:

$$E(s^{i}_{jt}) = \Pr(a^{i}_{jt}=1) \cdot E(s^{i}_{jt} \mid a^{i}_{jt}=1).$$

We model the probability of having any drug locally available using a model of entry proposed by Bresnahan and Reiss (1987, 1990, 1991a and 1991b). Any ARV drug is available locally if and only if the ex-ante expected value of offering that drug by at least one potential firm (whether the patent innovator and holder firm, or an imitator) is positive. That is, if the present discounted value of the flow of profits minus the fixed costs of entering the market for at least one firm is positive,

$$a^{i}_{jt}=1 \Leftrightarrow E[V(n^{i}_{jt} \geq 1)] = V(x,z,r;\theta_1) - F^{i}_{jt} > 0, \qquad (1)$$

where *V* denotes the value function (the present discounted value of the flow of profits of selling drug *j* in country *i* at time *t*) as a reduced form function of a set of *k* market shifters and profit drivers (x^{ik}_{jt}), a set of *l* instruments as explained below (z^{il}_{jt}), and the country-drug-year patent regime (r^{i}_{jt}) that is equal to one if the government of country *i* offers a patent right option to the developer of drug *j* at time *t*, and zero otherwise, and a set of parameters (θ_1). The reduced form value function (*V*) might be increasing or decreasing with respect the country-drug-year patent regime (r^{i}_{jt}). On one hand, patents prevent competition from imitators during the patent term, and therefore patents increase the flow of gross profits in those markets in which other firms would otherwise enter and compete with the innovator at some point of the patent term. On the other hand, obtaining and enforcing patents right is expensive for the patent owner. Patents increase the costs of marketing new drugs. Additionally, introducing a new drug in a developing country may imply a risk for global and innovative firms that market drugs in low price and high price markets: parallel traders might try to divert drugs back to high price markets when new and cheaper drugs become available in developing countries, or alternatively and with similar effect, consumers from high income markets might complain and ask for the lower prices offered in other countries.

F^{i}_{jt} is the annual fixed cost of marketing drug *j* in market *i* at time *t* : for instance, annual fixed production costs, annual fixed distribution costs, annual fixed promotional costs, annual fixed surveillance costs, expected annual fixed damage and liability costs, or even expected annual losses in high price markets due to parallel trading or consumers protest. Let us assume that F^{i}_{jt} is a log normal random draw corresponding to the annual fixed cost of marketing drug *j* in country *i* at time *t* that faces any potential entrant firm.

$$\ln F^{i}_{jt} = \mu^{i}_{j} + \sigma_{\varepsilon}\upsilon^{i}_{1jt}, \qquad (2)$$

$$\upsilon^{i}_{1jt} \sim N(0,1).$$

From the natural log of inequality 1 and from equation 2 we find that any drug *j* will be available at any country *i* at time *t* if and only if inequality 3 holds:

$$\ln V(x,z,r;\theta_1) - \mu^{i}_{jt} - \sigma_{\varepsilon}\upsilon^{i}_{1jt} > 0. \qquad (3)$$

Let us denote $V^*(x,z,r;\theta_2)$ the new reduced form expected net value function that takes into account the mean and the variance of the cost of introducing a new drug as follows,

$$V^*(x,z,r;\theta_2) = \frac{1}{\sigma_{\varepsilon}}\left[\ln V(x,r;\theta_1) - \mu^{i}_{jt}\right].$$

Then, any potential competitor will make available a new drug if and only if the following inequality holds,

$$V^*(x,z,r;\theta_2) - \upsilon^{i}_{1jt} > 0.$$

And then, the probability of having drug *j* available at country *i* at time *t* is the following,

$$\Pr(a^{i}_{jt} = 1) = \Pr\left(V^*(x,z,r;\theta_2) - \upsilon^{i}_{1jt} > 0\right) = \Phi\left(V^*(x,z,r;\theta)\right),$$

where Φ denotes the cumulative distribution of the standard normal.

That new reduced form inequality and the corresponding probability of having a new drug available can be used as the selection or participation inequality in a Heckman selection

model. Heckman (1976) outlines the estimation of parameters of equations with dependent variables that are only observed and then selected if an underlying inequality holds.

Finally, we model the market coverage, that is, the percentage of patients that are under a specific drug treatment in a given year and country (s^{i}_{jt}) as a function of country-drug-year patent regime (r^{i}_{jt}), a set of m observable exogenous drivers (x^{jm}_{jt}), and an unobservable mean zero and normally distributed random variable $\sigma_s \upsilon^{i}_{2jt}$,

$$s^{i}_{jt} = D(x, r; \beta) + \sigma_s \upsilon^{i}_{2jt}.$$

In this equation, υ^{i}_{2jt} is also a standard normal random draw. We allow to be potentially correlated with υ^{i}_{1jt}, with correlation coefficient equal to ρ. The correlation coefficient takes into account that the unobservable random part of the fixed cost of introducing a new drug in a particular country and year might be correlated with the unobservable random variable that defines the percentage of patients with access to that drug. For instance, the fixed costs of setting up the new facilities and training the new personnel at entry in the drug availability equation might be correlated with the unobservable demand drivers of the drug in the market coverage equation.

Summing up, we identify the effect of patents on expected market coverage, $E(s^{i}_{jt}) = \Pr(a^{i}_{jt} = 1) \cdot E(s^{i}_{jt} \mid a^{i}_{jt} = 1)$ using a system of two equations: (1) the likelihood of drug entry conditional on patent enforcement (reduced form probit selection equation, number 1 below); and, (2) the endogenously selected equation of market coverage as a function of the exogenously determined patent regime (equation number 2 below):

(1) $\Pr(a^{i}_{jt} = 1) = \Pr\left(V^{*}(x, z, r; \theta_2) - \upsilon^{i}_{1jt} > 0\right) = \Phi\left(V^{*}(x, r; \theta)\right)$

(2) $s^{i}_{jt} = D(x, r; \beta) + \sigma_s \upsilon^{i}_{2jt}$

(3) where, $Corr(\upsilon^{i}_{1jt}, \upsilon^{i}_{2jt}) = \rho$

We estimate the selection equation and the market coverage equation simultaneously using maximum likelihood techniques to obtain consistent and asymptotically efficient estimates of the parameters.

This approach of studying the impact of patents relies on four key assumptions: (1) that we have sample variation based not only on the endogenous variable, but also on the patent indicator under study across drugs and country pairs; (2) that we include control variables in the equations to avoid bias from omitted variables; and, (3) that the changes in the patent regime indicator and the control variables are exogenous; (4) that we appropriately take into account that the sample is endogenously determined.

First, our approach relies on having enough sample variation not only with respect to sales across country-year pairs, but also with respect to the patent regime across observations. The timing of drug discovery and the changes in the patent regimes across countries generates the variation of patent enforcement across drug-country pairs in the sample. Each drug-country specific patent regime depends on two dates: (1) whether and for how long patent protection was locally available for the drug innovation claimed; and, (2) whether patent protection must be locally available on account of World Trade Organization (WTO) member countries' obligations.

Time differences in implementing changes in national patent laws and the timing of the invention of HIV/AIDS drugs lead to an appropriate mix of patent regimes across drug-country pairs. Patent protection on pharmaceuticals changed substantially in some developing countries due to the World Trade Organization (WTO) Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS). Under TRIPS, WTO member countries are obliged to allow for the filing of product patents for pharmaceuticals by 1st January 1995. They subsequent should grant either product patents, or Exclusive Marketing Rights (EMR) until the applications of patent rights for eligible new drugs is granted or rejected.[3] Developing countries were allowed up to 1st January 2005, and least-developed countries up to 1st January 2006 (and now up to 2016 under the Doha Ministerial

[3] When product patents are not available in a WTO member country as for 1st January1995, WTO members have to provide a system whereby drug patent applications can be filed (often referred to as a "mailbox" system). "Mailbox" applications do not have to be examined until the local patent law is passed. However, when a drug subject to a "mailbox application" obtains marketing approval before the local patent office takes a decision on whether granting a patent right or not, the following special rule applies: An Exclusive Marketing Right (EMR) of up to five years (or until the patent is granted or rejected, whichever is shorter) must be granted from the date of local marketing approval, provided that a patent has been filed for that drug and a patent and marketing approval obtained in another WTO member country after 1st January 1995.

Declaration on the TRIPS Agreement and Public Health) to formally change patent laws to introduce pharmaceutical product patent protection.

In the countries not providing patents to eligible drugs before 1st January 1995, TRIPS obligations do not affect drugs that were no longer "new" for patenting purposes as on the date of filing in that country or as on the date of priority accorded to them upon request. An invention is considered to be new if it does not form part of the so-called "state of the art". The state of the art is generally defined as everything made available to the public by means of a written or oral description, by use, or in any other way, before the date of filing of the patent application. Under WTO rules, incorporating existing WIPO (World Intellectual Property Organization) conventions, for purposes of determining novelty, patent applicants may claim the priority of an earlier application made during the period of 12 months from the date of filing in order to preserve novelty. Therefore, we can conclude that all WTO Members would be obliged to make patents (or EMRs) available to inventions for which the first patent application was made in any WTO member on or after 1st January 1994. [4]

The key patent applications corresponding to the 15 ARV drugs were filed in the US between September 17th 1985 (Zidovudine, AZT) and June 2nd 1995 (Efavirenz). Therefore, we have a convenient pseudo-experimental mix of observations (country-drug pairs) for which patents rights may be claimed or not depending on the date of the key patent application (the priority date of the invention), and the date since when national governments made patent rights or EMR available to eligible drugs.

Second, our approach also relies on controlling for variables affecting the outcome apart from the patent indicator under study. In the regression analysis, we take care of omitted variables by controlling for relevant drug characteristics, and also country-year fixed effects. The empirical literature on drug markets draws our attention to the additional need

[4] While it is possible to obtain the priority dates for the basic product patents, it is not simple to determine which medicines are clearly out of the TRIPS-net and therefore ready to be copied in WTO Member countries. This is because the effect of subsequent patents belonging to the same drug group would depend on the scope of these later patent claims (new treatment dosages, new pharmaceutical forms, etc.). We have decided to include drugs that have priority date for the key patent before 1st January 1994 as outside the TRIPS-net or under the "no-patent regime" even if they have subsequent patents within the TRIPS-net. This would give the lower bound of the estimates we make, i.e. the lowest possible effect of the patent regime.

for controlling for differences in observed drug qualities such as dosage, efficacy, and side-effects.[5] Country-year pair effects should take into account cross country differences in access to health services and, particularly, access to free drugs programs such as those of Brazil and Thailand.

Third, the key underlying assumption in our study is that the patent regime, that is the patent status attainable for each drug in each country at any time, is exogenous with respect to the endogenous variables (market coverage and drug availability). We have shown above that patent law changes in the countries of our sample were driven mainly by bilateral or international agreements and national political developments, rather than by concerns related to the treatment of HIV patients with ARVs. It is an indicator that avoids the problem of endogeneity between firm's decisions to actually apply for patent protection in any country and the firm's decisions on entry, production, and pricing.

Finally, we observe sales of any drug in any given country only when at least one firm has decided to launch the drug in such a country. As drug availability depends on the expected sales, drug availability is endogenously determined. We take care of bias caused by the fact that our observations are drawn non-randomly conditionally on patent enforcement corresponding to each drug-country pair by using Heckman's selection model. This model is very convenient but it has also drawbacks. The estimates and test statistics we will use are sensitive to the distributional assumptions made regarding the error terms $(\upsilon^i_{1jt}, \upsilon^i_{2jt})$ and to the assumed functional form of the market coverage equation. This critique applies most forcefully if we have no valid instruments in the selection equation. In this case, identification is achieved only through the functional-form assumption. A set of instruments in the selection equation makes the identification more robust, as the instruments are excluded from the market coverage regression.

[5] The empirical literature that studies specific drug markets shows that we should control for dosage, efficacy, toxicity, and side-effects among other observed qualities: Berndt, Griliches and Rosset (1993) study antihypertensive drugs; Berndt *et al.* (1995), and Berndt, Pindkyck and Azoulay (1999 and 2000) focus on antiulcer drugs; Berndt, Cockburn and Griliches (1996) analyze antidepressant drugs; and Cockburn and Anis (1998) arthritis drugs. We do not have enough data on differences in drug toxicity among ARVs although higher life-threatening toxicity has been related to the use of a type of ARV, the so-called Nucleoside Reverse Transcriptase Inhibitors (NRTI). Therefore, we rely on drug fixed effects to take care of fixed differences in toxicity across drug types.

We include as control variables in the selection equation convenient instruments that explain the likelihood of entry and that are exogenously given with respect to market coverage to make our identification more robust. We use the sum of their characteristics (constant term, dosage, efficacy and adverse reactions).[6] That is, for any given drug *j*, country *i*, year *t*, and characteristic *l* we construct an instrument z_{jt}^{il} summing the characteristic *l* across all drugs *g* different from *j* that are available in the choice set of drugs in the US at the given year, J_t^{US}:

$$z_{jt}^{il} = \sum_{j \in J_t^{US} g \neq j} x_g^l$$

We are safe to assume that the variation of the sum of characteristics of all potential competitor drugs in the US choice set is exogenously given by the stream of innovative activity mostly in Europe and the US, and is not given by the likelihood of introduction of drugs across countries and years, neither by the expected market coverage. However, it is sensible to assume that the expected drug availability will depend on whether there is the potential threat of entry (if the drugs are substitutes) or benefit from entry (when the drugs are complements) by one or more firms marketing other HIV/AIDS drugs.

2.2 Data

Treatment of AIDS in rich countries changed dramatically after 1995, when new, more effective, and safer drugs were approved. According to Henkel (1999), the combination of the new drugs with the older ones (Highly Active Antiretroviral Therapy, HAART, or "cocktail therapy") 'has helped change AIDS in the last three years from being an automatic death sentence to what is now often a chronic, but manageable, disease'. As Table 1 shows, 14 different drugs containing one molecule, and one drug combining two molecules (i.e. a total of 15 drugs), were available in the US by June 2000.

IMS, the leading collector of data on drug sales world-wide, provided us with annual sales data for these 15 ARVs in 21 different countries and two country groupings, viz.

[6] The instrument vector summing the constant term of the US choice set offers the variation of the number of potential drug competitors across drugs and years, and the sum of dosage, efficacy and adverse effects of the drugs in US choice set offers the variation of the characteristics of all potential competitors across drugs and years.

French West Africa and Central America, between 1995 and 1999.[7] As noted earlier, there were no significant discounts given by patent owners of these drugs in this period.

IMS data consist of annual wholesale sales and revenues estimates corresponding to each particular drug presentation sold at retail outlets between 1995 and 1999, except in 4 cases. IMS reports total aggregated retail and hospital sales (R&H) in South Africa, Thailand, the Philippines and Indonesia.

IMS data refer only to sales. They do not include free distribution of drugs to patients, nor do they include any donations of drugs. This is particularly important in Brazil. The Brazilian government provides free access to ARV therapy to HIV patients and produces many of the ARVs in public sector facilities or imports them directly from the manufacturers. Thailand also has a substantial public distribution programme. However, except for Brazil and Thailand, it seems that such programmes were treating a tiny number of patients in our sample of countries and during our sample period, 1995-1999. Unfortunately, we do not have year-wise data on such free distribution of drugs. It is worth emphasizing that the results of our research refer only to actual drug sales.

2.3 A First Look at Market Coverage, Availability, Patent Regime, and Covariates

Patent Rights across Countries and Drugs

Before January 1st 1995, 12 countries or country groupings in our sample did make available the grant of product patents: the countries of Central America and the countries grouped under the heading of French West Africa, and also Malaysia, the Philippines, South Africa, Mexico, Thailand, Chile, Indonesia, and the members of the Andean Community (Ecuador, Peru, and Venezuela).[8]

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[7] IMS Health provided us with aggregated sales data for two supranational entities: French West Africa, comprising aggregate sales in Benin, Cameroon, Democratic Republic of Congo, Ivory Coast, Gabon, Guinea and Senegal; and, Central America, including Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua and Panama. All economic indicators for those two supranational entities are population weighted averages of the national indicators.

[8] Product patents for drugs have been granted in all Central American countries since the 1950s, except in Guatemala where product patents were introduced in 2000. Product patents for drugs were granted also in all French West African nations of our sample since the 1960s, except in Guinea

On the other hand, before January 1st 1995, 11 countries in our sample did not allow the grant of product patents: Argentina, Bangladesh, Brazil, Colombia, Dominican Republic, Egypt, India, Morocco, Pakistan, Tunisia and Uruguay.[9] Between 1996 and 2000, seven of those countries introduced patent protection for pharmaceuticals: Colombia in 1996; Brazil in 1997; Argentina in 1999; Morocco in 2000; and, Dominican Republic, Tunisia and Uruguay in 2001.[10]

The key patent applications corresponding to the 14 ARV molecules were filed between September 17th 1985 (Zidovudine, AZT) and June 2nd 1995 (Efavirenz).[11] Using a variety of sources, including local legislation, the complete cross-country data-set compiled by Qian (2001), and data from the WTO country-by-country intellectual property law reviews we obtained the date from which patent protection for pharmaceuticals could have been granted for each drug in each one of the 23 countries or country groupings of our sample.

We built up the patent regime indicator corresponding to each drug-country pair using the drug key patent priority date and the date from which each country could have granted patent protection. For each drug-country-pair, we assessed whether product patents would have been available locally within a year from the key priority date of each molecule.

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where product patents were also introduced in 1991. We set the patent regime indicator to be equal to 1 in all the country-drug-pairs corresponding to the two supranational entities.

[9] Pakistan had a patent law in force, but an executive order disallowed pharmaceutical patents. Dominican Republic had a patent law in force since 1911, but apparently the Ministry of Health was granting marketing approval for products that were infringing pharmaceutical patents until the new law came into force in 2001. Bangladesh has a patent law in force since 1985 which does not exclude pharmaceutical products from patentability, however it is unclear whether patents for pharmaceutical were granted or enforced since then.

[10] We focus on product patents (exclusivity related to therapeutically active ingredient) rather than process patents (exclusivity related to the method of obtaining such active ingredient). Process patents, like other type of patents on therapeutic uses, pharmaceutical forms, and so on, are important but concomitant ways of protecting the main and broader exclusivity right of the innovator, that protecting the therapeutic active ingredient from being copied and sold.

[11] The US Federal Food, Drug, and Cosmetics Act require that drug firms provide patent information with all new drug applications. Taking into account this information, the FDA sets the exclusivity term during which an abbreviated new drug application is not granted (a generic is not approved). The *Electronic Orange Book* (FDA, 2000) publishes the number of the appropriate patents claimed by the firms when the drugs are subject to approval. Using the patent numbers, Balasubramaniam (2000) obtained each ARV key priority date from the US Patent and Trademark Office online database. We thank Mike Palmedo from the Consumer Project on Technology for explaining to us how this data was gathered.

Additionally, TRIPS provisions on EMRs affect four of the 14 ARV molecules.[12] Of the drugs in our sample, these four drugs fall into the "TRIPS-net". For the following four molecules, we estimate that patent applications could have been filed after January 1st 1995 in all WTO countries apart from the country where the patent was first filed : Nelfinavir (basic patent priority date - February 2nd 1994); Delavirdine (basic patent priority date – February 22nd 1994); Ritonavir (basic patent priority date - April 25th 1995); Efavirenz (basic patent priority date - June 2nd 1995). We set the patent regime indicator to be 1 for these four drugs in all countries in our sample because local governments would be obliged to provide EMR or product patents to the innovators of these molecules under TRIPS rules.

We refer to that patent status attainable, as the country-drug pair "patent regime." The patent regime indicator does not report whether the innovator was granted or had even applied for patent protection for each drug-country-pair of our sample. In other words, it does not reflect the actual patent status of the drug. It only shows that patent or other market exclusivity status was attainable, to the best of our knowledge. So, the patent regime is exogenous to firm decisions. Taking into account the value of patent protection, innovators may decide whether or not it pays to apply in each one of the countries that make available such rights. This we consider to be a relevant variable in view of the criticism directed against the TRIPS rules that the existence of such obligations lead to lowered access to essential drugs in developing countries.

Table 2 shows that Central America, French West Africa, Malaysia, the Philippines and South Africa led the sample in the number of drugs for which patents could have been granted by 1999. In these five countries or country groupings, the patent holders of all 15 drugs could have applied for patents. In a second set of countries, patent laws have changed recently to make product patents available for pharmaceuticals: Mexico (1991), Thailand (1992), Chile (1991), Indonesia (1991), Ecuador (1994), Peru (1994) and Venezuela (1994). Mexico and Thailand led this second group of countries because they granted the so-called 'pipeline' protection when introducing legislation on product patents. In these countries, innovators could apply for patent protection or market exclusivity for drugs in the 'pipeline', i.e. drugs not already marketed although not 'new' for patenting, when the new law came

[12] See Articles 70.8 and 70.9 of the TRIPS Agreement.

into force. Finally, in 11 countries in our sample, innovators could only apply for patents or EMRs for the 4 drugs affected by the TRIPS rules on 'mailbox applications'.

Drug Availability across Countries and Years

Table 2 also shows that local availability of drugs in the local markets varies substantially across countries and years. The most striking feature of the distribution of the data is that only six countries or country groupings had 10 or more drugs available by 1999: Argentina, Chile, Colombia, Thailand, Mexico and South Africa. Except for Chile, this set of countries had most drugs available soon after they were available in the US. A second group of seven countries or country groupings had only between 5 and 9 drugs by 1999: French West Africa, Brazil, Malaysia, Uruguay, Central America, India and Venezuela. The remaining ten countries had only 4 or fewer drugs available by 1999.

Sales across Countries and Years

Table 3 shows the distribution of drug sales in terms of equivalent annual single-drug therapies by country and year. By 1999, Thailand was leading the table of countries by sales: 6,986 out of the 15,666 total single-drug therapies were sold in Thailand. We note that Brazil ranks 9th in this table although most HIV/AIDS patients needing therapy were able to access free drugs through the public sector. IMS report zero sales for Bangladesh, Morocco, Pakistan or Tunisia during this period.

Using the sales data, we estimated how many patients actually in need of therapy had access to for-profit ARV treatment. As Henkel (1999) pointed out, 'some HIV-infected patients progress to AIDS quickly while others can remain healthy for 10 years or more'. We used the estimated numbers of patients living with HIV in each country to turn the access problem into a relative measure.

Assuming that about 10% of those living with HIV are urgently in need of ARV therapy, we divided the number of annual single-drug therapies sold by the number of

patients in need of cocktail therapy.[13] Table 4 shows that even by this low standard by 1999 only the equivalent of 1.21% patients in need of ARV therapy had access to a single-drug annual therapy in our sample. Only Argentina (19%), Malaysia (17%) and Colombia (15%) had percentages of access of 15% or more. Thailand, including retail and hospital sales, reached 9.25% in 1999, and Chile (6.21%) and Mexico (4.98) had figures close to 5%. The Philippines (2.07%) and Indonesia (1.36%), both including retail and hospital sales, had figures slightly above the weighted average (1.21%), and the remaining countries had percentages below that average.

The estimates for Brazil show that sales increased from 1995 to 1996 and then decreased. This data is consistent with the increasing number of patients treated within the public program which was launched in 1996. According to the Brazilian Ministry of Health (2002), an increasing number of patients (35,900 in 1997, 65,000 in 1998 and 73,000 in 1999 of the estimated 540,000 HIV Brazilian patients or roughly 12-13%, thus exceeding our standard of 10%) had access to the free drug program. It is clear that from 1997 on an increasing number Brazilian patients did not need to buy their ARV drugs from the market.

Mean Differences across Patent Regimes

Finally, we take a first look at how market coverage, availability and other covariates vary across patent regimes. Table 5 shows the mean and standard deviations of market coverage, the number of years since the drug was launched in the US, the number of competitor firms offering the same drug, and drug availability across our 1,273 country-drug-year triplets grouped according to the binary indicator of patent regime.

The first column of table 5 offers the mean and standard deviations of those variables for our entire sample. Columns 2-3 split all the observations of the sample according to the drug patent regime. Column 5 shows the means and standard deviations for a selected sample of those observations for which drugs actually became available. Columns 6-7 split this selected sample according to the drug patent regime again. Columns 4 and 8 report the p-values for equal means test across patent regimes. This test should be

[13] Dr. Paul Farmer suggested to the authors that at least around 10% of the HIV patients in the Central Plateau of Haiti should be treated. See Farmer *et al* (2001).

interpreted just as a convenient way of describing the data and should not be used for inference purposes.

Let us look first at the entire sample. Patent regime is associated with smaller mean percentage of AIDS patients on each specific drug --market coverage-- (0.12% vs. 0.19%); patent regime is also associated with a shorter delay in availability from the date since the drug is launch in the US (2.72 years vs. 4.23 years); and, patent regime is also associated with less competitors per drug (0.31 vs. 0.41). By contrast, drug availability does not seem to vary systematically with patent regime.

Let us now turn to the selected sample of observations for which drugs actually became available. The observed differences in the means are even larger than before. Mean percentage of AIDS patients on each specific drug (market coverage) reaches 0.39% under patent regime while it is 0.73% under no patent regime; mean years since launch in the US is 4.78 under patent regime while it is 5.90 under no patent regime; and, mean number of competitors is 1.02 while it is 1.56 under no patent regime. Under patent regime, the number of competitor is usually one, and exceptionally two. The global innovator of the drug and patent holder is the only firm that launches the drug, but in a couple of observations a Canadian generic competitor also enters the market more than 10 years after the drug was launched in the US. Under no patent regime, the global innovator of the drug is the first firm to enter the market, and in many markets local firms use to launch a bit later copy products of the same drug.

Apart from the differences across patent regimes, it is worth noting that patentability is 43% in the entire sample while it is a bit larger for the selected sample covering only the drugs that are actually available, 52% (see columns 1 and 5). Also, the differences in market coverage across patent regimes are statistically significant but not very large. It is only 0.07 percentage points for the entire sample, while it reaches 0.34 percentage points for the selected sample including only the observations for which drugs are actually available.

3 Results

The first column in Table 6 shows the results of a preliminary regression of market coverage (the log of the percentage of AIDS patients that consume an annual single-drug ARV treatment in each drug-country-year market) on the country-drug-year triplet patent regime dummy. We control for drug heterogeneity by including a set of drug characteristics (drug type, dosage, efficacy, adverse reactions, and the first order and the second order effect of the number of years since the drug was launched in the US). We include country-year pair fixed effects for taking care of other country and time specific variations (such as tariffs, prices regulations, access to health care, and so on).

The second column in Table 6 shows the results of a preliminary probit model which shows the effect of a set of country and drug characteristics on the probability of having the sample mean HIV/AIDS drug available across countries and time. We allow the patent regime dummy to interact with the number of years since launch in the US because as we have just seen in the previous section there are not significant differences in mean availability across patent regimes. We control for drug heterogeneity by including a set of drug characteristics (drug type, dosage, efficacy, adverse reactions, and the first order and the second order effect of the number of years since the drug was launched in the US). We control for cross country and year variations using mean income, income inequality and year fixed effects instead of country-year pair fixed effects to avoid predicting some outcomes perfectly.

The third and fourth columns of Table 6 show the results of the selection model including the simultaneous estimation of the market coverage equation and the drug availability equation. In the drug availability equation, we include the covariates of the preliminary probit and we also include our instruments as controls for making our model specification more robust and less vulnerable to the functional form assumptions. As explained above, we control for the sum of the characteristics of all alternative drugs already launched in the US (heterogeneity of potential competition). In the market coverage equation we include the covariates of the preliminary OLS market coverage regression.

The preliminary regression in the first column of Table 6 shows that the drug-country patent regime has a negative but not statistically significant effect on market

coverage at the conventional 5% level (coefficient of -0.75, and standard error of 0.52). This result implies that on an average, market coverage is 53% smaller when drugs are sold under patent regime than when those drugs are sold under a no patent regime.[14] However, this result is poorly measured and biased because of the selection of the sample.

The second column of table 6 shows that drug availability depends on the interaction between the patent regime and the life cycle of the product. Patent has a negative and significant effect on drug availability at the 1% level (coefficient of -1.38 and standard error of 0.40). But also, the interaction between the patent regime indicator and the variables that measure the years since the drug has been launched in the US have significant impact on drug availability at the 1% and 5% level respectively (first order coefficient of 0.62 and standard error of 0.19, and second order coefficient of -0.03 and standard error of 0.01). Table 7 shows how on average patents reduce the probability of having a sample mean drug until the second year after the drug is launched in the US (by 35, 20 and 6 percentage points in each year), but that patents increase availability thereafter by more than 25 percentage points between the fifth and the twelfth year after the drug was launched in the US.

The third and fourth columns of table 6 allow us to disentangle the effect of the patent regime on drug availability and the effect of patent regime on sales. The coefficient of the patent regime in the market coverage equation increases in absolute value and turns to be statistically significant at the 1% level (coefficient -0.89 and standard error of 0.36). This result implies market coverage is on average 59% smaller when drugs are sold under a patent regime than when those drugs are sold under a no patent regime conditional on having the drug available.[15] However, this negative effect of the patent regime might be reinforced or moderated by the effect of the patent regime on drug availability. The effect is indeed reinforced by the negative effect of the patent regime on drug availability during the early life cycle of the product. At the time the drug is launched in the US, the patent regime has a negative and statistically significant effect on drug availability. However, after a couple of years after the drug is launched in the US, being under patent regime increases the probability of having the drug locally. Therefore, after a couple of years, patents increase the

[14] exp(-0.75)-1.

[15] exp(-0.89)-1.

probability of having the drug available. This effect is counterbalancing the negative effect of patents on the market coverage regression latter in the life cycle of the product. Switching all drugs from a no-patent to a patent regime increases mean availability by five percentage points, from 28% to 33%.

The parameter estimates of the model shown in Table 6 allow us to predict the net impact of any change in the patent regime on sales. We obtain an estimate of the unconditional expected access to drug therapy by multiplying the estimates of the probability of having an ARV drug available (column 4 in Table 6), by the conditional expected access to that ARV drug (column 3 in Table 6):

$$E(s_{jt}^{i}) = \Pr(a_{jt}^{i} = 1) \cdot E(s_{jt}^{i} \mid a_{jt}^{i} = 1)$$

Table 8 shows the change in the predicted number of single-drug annual treatment doses when we switch all drugs in the sample that are currently subject to a patent regime to a no-patent regime. This is like waiving the patent rights actually in place, as for example, through the systematic grant of compulsory licenses.

The impact of changing to a no-patent from a patent regime would have been an increase on sales for the 5-year period by as much of 14,158 annual therapies. As Table 8 shows, this is an increase of 34% in market coverage, that is, an increase of 0.30 percentage points from the tiny 0.88% of actual coverage to market coverage of 1.18%. It appears that patent rights do matter but patents cannot be blamed for the lack of access of the vast majority of patients in developing countries because even without patents market coverage would have only reached 1.21% in 1999.[16]

Table 9 shows the impact on total market coverage by country when we switch all drugs currently under patent regime to a no-patent regime. The results are heterogeneous by country. On one hand, the number of drug annual treatment doses increases strongly in countries such as Thailand (9,858 annual treatment doses) and South Africa (2,245 annual

[16] We have checked the robustness of our results with respect to the Dominican Republic as it is a a country offering patent rights to all drugs but according to the a poorly enforced 1911 law. Results do not differ strongly and are available from the authors upon request. We have also checked the robustness of our results with respect to Bangladesh since there is uncertainty regarding its patent regime. Again, results do not differ strongly when we set all drugs in Bangladesh as if patents were actually granted and enforced.

treatments). Those two countries have most of the drugs under patent regimes, and then would benefit the most from a patent waiving program. After them, the number of annual treatment doses increases substantially in Argentina (958), Mexico (763) and to lesser extent Malaysia (492).

On the other hand, sales would have been substantially smaller without patent rights in Central American and French West Africa. In those two regions all drugs are under patent regime, and the predictions suggest that waiving the patent right might do more harm than good. In all those countries, patents are actually increasing access because the positive effect of patents on availability offsets the negative effect of patents on sales due to the softer competition. Table 10 shows that in Central American patents increases mean drug availability from 20% to 29% and in French West Africa from 6% to 15%. Although this may seem counter-intuitive, one explanation could be that with patents available, the originator firms have an incentive to market their product in order to capture the niche upper-income segment of the population of patients even in very poor countries. Table 10 also shows that patents have a positive impact on mean availability in most countries except in Argentina where the predicted mean availability would decrease from 62% to 56% if we switch all drugs from a no-patent to a patent regime, and in South Africa where the predicted mean availability would decrease from 77% to 67% when switching all drugs from no-patent to patent regime.

4 Conclusions

This paper offers for the first time an estimate of exclusion from access to new HIV/AIDS drugs in poor countries. Only 1.21% of the patients urgently in need of new drugs were able to afford the high local prices of a single new drug therapy in 1999. The vast majority of patients suffered from not having the new drugs locally available. Only in a very select group of poor countries were the new drugs locally available soon after they were launched in the US.

The main finding of the paper is that patents do constrain sales of new drugs in developing countries. We found that the net impact of having patent regimes on expected sales in the developing countries of our sample is significant. Switching all drugs to a no-

patent regime would increase access to treatment with even one new ARV drug by 34% between 1995 and 1999: from 0.88% to only 1.18%. However, even switching all drugs from patent to no-patent regime would have excluded the vast majority of patients from therapy.

This evidence suggests that apart from the effects of patents on producer surplus and incentives to innovate, patents have a strong impact on availability of drug therapy and access to drug therapy in developing countries. Patents have a negative net effect on mean access to therapy. This effect is caused by the strong effect of patents on the competition of drug firms in the market place (patent holders do not face the stiff competition from imitators), and this effect is only partially offset by the positive impact of patents on mean drug availability in developing countries.

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6 Tables

Table 1.- ARVs approved in the US by June 2000 (from older to newer in the US)

Molecule generic name	Drug type	Brand name in the US	Firm name in the US	Basic priority date of the earliest patent application	Launch Year in the US
ZIDOVUDINE (AZT)	NRTI	Retrovir ®	Glaxo Wellcome	March 16, 1985	1987
DIDANOSINE (DDI)	NRTI	Videx ®	Bristol-Myer	August 11, 1987	1991
ZALCITABINE (DDC)	NRTI	Hivid ®	Roche Labs	January 13, 1987	1992
STAVUDINE (D4T)	NRTI	Zerit ®	Bristol-Myer	December 17, 1986	1994
LAMIVUDINE (3TC)	NRTI	Epivir ®	Glaxo Wellcome	February 8, 1989	1995
SAQUINAVIR	PI	Invirase ® and Fortovase ®	Roche Labs	December 11, 1989	1995
INDINAVIR	PI	Crixivan ®	Merck	May 7, 1993	1996
NEVIRAPINE	NNRTI	Viramune ®	Roxane	July 03, 1993	1996
RITONAVIR	PI	Norvir ®	Abott Pharm	April 25 , 1995	1996
DELAVIRDINE	NNRTI	Rescriptor ®	Agouron	February 22, 1994	1997
LAMIVUDINE & ZIDOVUDINE	NRTI	Combivir ®	Glaxo Wellcome	March 16 1985	1997
NELFINAVIR	PI	Viracept ®	Agouron	February 2, 1994	1997
ABACAVIR	NRTI	Ziagen ®	Glaxo Wellcome	June 27, 1988	1998
EFAVIRENZ	NNRTI	Sustiva ®	Du Pont Pharm.	June 2, 1995	1998
AMPRENAVIR	PI	Agenerase ®	Glaxo Wellcome	September 7, 1993	1999

Source: PDR (2000), Balasubramaniam (2000), and FDA (2000).

Table 2.- Number of drugs available
(Number of drugs for which the innovator could obtain patent or exclusive marketing rights)

	1995	1996	1997	1998	1999
US	**6 (6)**	**9 (9)**	**12 (12)**	**13 (14)**	**15 (15)**
ARGENTINA	4 (0)	7 (1)	10 (3)	12 (4)	14 (4)
CHILE	0 (1)	1 (4)	5 (6)	9 (7)	12 (8)
COLOMBIA	1 (0)	4 (1)	6 (3)	10 (4)	12 (4)
THAILAND R&H	3 (4)	6 (7)	8 (10)	10 (12)	12 (13)
MEXICO	3 (5)	3 (8)	5 (11)	8 (12)	10 (13)
SOUTH AFRICA R&H	3 (6)	4 (9)	6 (12)	9 (14)	10 (15)
FRENCH WEST AFRICA	2 (6)	2 (9)	4 (12)	8 (14)	9 (15)
BRAZIL	1 (0)	4 (1)	4 (3)	5 (4)	7 (4)
MALAYSIA	1 (6)	2 (9)	5 (12)	6 (14)	7 (15)
URUGUAY	1 (0)	1 (1)	1 (3)	5 (4)	7 (4)
CENTRAL AMERICA	1 (6)	1 (9)	4 (12)	5 (14)	5 (15)
INDIA	n.a (0)	n.a (1)	1 (3)	2 (4)	5 (4)
VENEZUELA	0 (0)	0 (3)	2 (5)	3 (6)	5 (6)
PHILIPPINES R&H	1 (6)	2 (9)	2 (12)	3 (14)	4 (15)
DOMINICAN REPUBLIC	0 (0)	0 (1)	0 (3)	0 (4)	3 (4)
ECUADOR	0 (0)	1 (1)	1 (3)	1 (6)	3 (6)
PERU	0 (0)	0 (3)	1 (5)	3 (6)	3 (6)
INDONESIA R&H	1 (1)	3 (4)	4 (6)	2 (7)	2 (8)
BANGLADESH	0 (0)	0 (1)	0 (3)	0 (4)	0 (4)
EGYPT	0 (0)	0 (3)	0 (5)	0 (4)	0 (4)
MOROCCO	0 (0)	0 (1)	0 (3)	0 (4)	0 (4)
PAKISTAN	0 (0)	0 (1)	0 (3)	0 (4)	0 (4)
TUNISIA	0 (0)	0 (1)	0 (3)	0 (4)	0 (4)

n.a.: no data available. R&H: Retail & Hospital sales. Otherwise, retail sales only. French West Africa comprises Benin, Cameroon, Democratic Republic of Congo, Ivory Coast, Gabon, Guinea and Senegal. Central America includes Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua and Panama.

Source: Authors' calculations based on IMS, local legislation, Balasubramaniam (2000), Qian (2001), and WTO legislative reviews.

Table 3.- Sales of equivalent full year single-drug ARV treatment doses (in actual numbers)

	1995	1996	1997	1998	1999	2000[1]
THAILAND R&H	653	1,533	5,028	5,502	6,986	7,790
SOUTH AFRICA R&H	78	81	195	511	2,196	3,371
INDIA	n.a.	n.a.	88	45	417	2,414
ARGENTINA	305	748	2,102	2,622	2,481	2,284
MEXICO	288	337	506	1,148	747	1,528
COLOMBIA	2	36	405	704	1,056	937
MALAYSIA	1	13	103	582	848	706
FRENCH WEST AFRICA	8	14	30	165	434	528
BRAZIL	83	1,020	413	164	124	163
INDONESIA R&H	5	15	11	8	71	110
CHILE	0	0	5	65	93	93
CENTRAL AMERICA	2	4	23	22	82	91
PHILIPPINES R&H	6	11	25	40	58	63
VENEZUELA	0	0	120	83	42	32
ECUADOR	0	0	0	1	21	25
PERU	0	0	1	6	8	7
DOMINICAN REPUBLIC	0	0	0	0	1	2
URUGUAY	0	0	0	1	2	1
BANGLADESH	0	0	0	0	0	0
MOROCO	0	0	0	0	0	0
PAKISTAN	0	0	0	0	0	0
TUNISIA	0	0	0	0	0	0
Total	1,430	3,810	9,055	11,669	15,666	20,143

[1] July 1999 to June 2000. n.a.: no data available. R&H: Retail & Hospital sales. Otherwise, retail sales only. French West Africa comprises Benin, Cameroon, Democratic Republic of Congo, Ivory Coast, Gabon, Guinea and Senegal. Central America includes Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua and Panama.

Source: Authors' calculations based on IMS Health, WHO (2000) and PDR-CG (2000).

Table 4.- Sales of full year single-drug treatment doses out of AIDS patients (%)

Country	1995	1996	1997	1998	1999
ARGENTINA	4.03	7.85	17.52	20.99	19.08
MALAYSIA	0.03	0.24	1.51	10.08	17.30
COLOMBIA	0.03	0.60	5.62	9.85	14.88
THAILAND R&H	0.90	2.04	6.45	7.17	9.25
CHILE	0.00	0.01	0.32	4.20	6.21
MEXICO	1.49	1.81	2.81	6.98	4.98
PHILIPPINES R&H	0.31	0.49	1.03	1.56	2.07
INDONESIA R&H	0.10	0.29	0.21	0.15	1.36
ECUADOR	0.00	0.01	0.01	0.05	1.09
VENEZUELA	0.00	0.00	1.46	1.17	0.68
SOUTH AFRICA R&H	0.07	0.05	0.07	0.15	0.52
CENTRAL AMERICA	0.02	0.03	0.21	0.15	0.42
URUGUAY	0.01	0.04	0.04	0.19	0.32
BRAZIL	0.15	1.79	0.71	0.29	0.23
FRENCH WEST AFRICA	0.00	0.01	0.01	0.07	0.17
PERU	0.00	0.00	0.01	0.10	0.16
INDIA	n.a.	n.a.	0.02	0.01	0.11
DOMINICAN REPUBLIC	0.00	0.00	0.00	0.00	0.01
Total	0.20	0.43	0.78	0.96	1.21

n.a.: no data available. R&H: Retail & Hospital sales. Otherwise, retail sales only. AIDS patients are computed as the 10% of all HIV infected persons in any country and year. French West Africa comprises Benin, Cameroon, Democratic Republic of Congo, Ivory Coast, Gabon, Guinea and Senegal. Central America includes Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua and Panama.

Source: Authors' calculations based on IMS, WHO (1995), UNAIDS/WHO (1998 and 2000a).

Table 5.- Means (and standard deviations) of selected variables across patent regimes

	Entire sample				Selected sample: Only observations for which drugs are actually available			
	(1) All	(2) No Patent Regime	(3) Patent Regime	(4) Equal Means Test (2) vs. (3)	(5) All	(6) No Patent Regime	(7) Patent Regime	(8) Equal Means Test (6) vs. (7)
Market Coverage (%)	0.16 (0.62)	0.19 (0.67)	0.12 (0.56)	0.035	0.56 (1.06)	0.73 (1.13)	0.39 (0.96)	0.003
Years Since Launch in the US	3.49 (3.04)	4.23 (3.38)	2.72 (2.40)	0.000	5.32 (3.40)	5.90 (3.73)	4.78 (2.96)	0.001
Competitors	0.36 (0.80)	0.41 (1.01)	0.31 (0.47)	0.015	1.28 (1.03)	1.56 (1.43)	1.02 (0.13)	0.000
Availability	0.28 (0.45)	0.27 (0.44)	0.30 (0.46)	0.143				
Patent Regime	0.43 (0.49)				0.52 (0.50)			
Observations	1,273	655	618		363	175	188	

In (4) and (8) we show the probability (*p*-value) of falsely rejecting equal means in the above mentioned groups under the maintained hypothesis of equal variances.

Source: Authors' calculations based on IMS, local legislation, Balasubramaniam (2000), Qian (2001), and WTO legislative reviews.

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Table 6.- Market Coverage and Availability on Patent Regime. Coefficient (Standard Errors)

	Preliminary Regressions		Selection Model	
	(1) Market Coverage (OLS)	(2) Drug Availability (Probit)	(3) Market Coverage	(4) Drug Availability
Patent	-0.75 (0.52)	-1.38 (0.40)**	-0.89 (0.36)**	-1.72 (.55)**
Patent * Years in the US	-- --	0.62 (0.19)**	-- --	0.74 (0.24)**
Patent * Years in the US	-- --	-0.03 (0.01)*	-- --	-0.04 (0.02)*
Years in US	0.51 (0.13)**	0.22 (0.11)*	0.24 (0.13)+	0.18 (0.11)+
Years in US ^2	-0.04 (0.01)**	-0.005 (0.007)	-0.02 (0.01)*	-0.001 (0.01)
Mean Income (PPP$ 1,000)	-- --	0.24 (0.07)**	-- --	0.21 (0.05)**
Income Inequality (% Gini)	-- --	0.03 (0.02)	-- --	0.03 (0.01)*
Dosage	2.20 (0.66)**	-0.56 (0.19)**	2.60 (0.96)**	-1.20 (0.41)**
Efficacy	1.16 (0.29)**	0.05 (0.02)**	0.91 (0.33)**	0.09 (0.04)+
Adverse Reactions	0.29 (0.16)	-0.11 (0.02)**	0.48 (0.17)**	-0.08 (0.03)*
Lambda			-1.75 (0.32)**	
Characteristics Other Drugs	No	No	No	Yes
Drug Type Fixed Effects	Yes	Yes	Yes	Yes
Country-Year Pair Fixed Effects	Yes	No	Yes	No
Observations	363	1,273	363	1,273
R^2, Pseudo R^2 or Log likelihood	0.75	0.40	-956.27	

The hypothesis that each coefficient is zero is rejected at the two-sided 1% (**), 5% (*), or 10% (+) significance level respectively. Hospital sales fixed effects included. Dosage, Efficacy and Adverse Reactions in Logs in the equation (1) and (2) and in levels in the other equations (3). Robust Standard Errors Clustered on Country.

Source: Authors' calculations based on IMS, local legislation, Balasubramaniam (2000), Qian (2001), WTO legislative reviews, WHO (1995), UNAIDS/WHO (1998, 2000 and 2001), PDR (2000), PDR-CG (2000), UNDP/UNU/WIDER (2000), World Bank (2000a) and IMF (2001).

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Table 7.- Estimated Impact of Patent on Availability
Probit Estimates
(Change in the Predicted Probability, in percentage points)

Years	0	1	2	3	4	5	6	7	8	9	10	11	12
Patent Impact	-35	-20	-6	6	16	25	32	38	42	44	45	44	42

Source: Authors calculations based on table 6 estimates.

Table 8.- Impact of Switching All Drugs Currently in Patent Regime to No-Patent Regime

	1995	1996	1997	1998	1999	Total
Absolute Increase:						
In Sales	11	3827	5555	3154	1611	14158
In Market Coverage	0.002%	0.66%	0.48%	0.26%	0.12%	0.30%
Relative Increase:						
In Sales	0.8%	100.4%	61.3%	27.0%	10.3%	34.0%
Pro-memoria:						
AIDS Patients	471,388	581,956	1,155,960	1,212,596	1,289,388	4,711,288
Current Sales	1,430	3,810	9,055	11,669	15,666	41,630
Predicted Sales (No Patent)	1441	7637	14610	14823	17277	55788
Current Market Coverage	0.20%	0.43%	0.78%	0.96%	1.21%	0.88%
Predicted Market Coverage (No Patent)	0.31%	1.31%	1.26%	1.22%	1.34%	1.18%

Source: Authors' calculations based on table 6 estimates.

Table 9.- Prediction of the change in the annual treatment doses when we switch all drugs **currently** under patent regime to no-patent regime

	1995	1996	1997	1998	1999	Total
ARGENTINA	0	57	261	384	257	958
BANGLADESH	0	0	0	0	0	0
BRAZIL	0	119	47	22	9	197
CENTRAL AMERICA	**-1**	**-3**	**-10**	**-2**	**-54**	**-71**
CHILE	0	0	1	39	19	60
COLOMBIA	0	0	28	53	35	117
DOMINICAN REPUBLIC	0	1	3	16	0	20
EGYPT	0	0	0	0	0	0
EQUADOR	**0**	**0**	**0**	**0**	**-1**	**-1**
FRENCH WEST AFRICA	**-9**	**-6**	**-7**	**-188**	**-325**	**-535**
INDIA	n.a.	n.a.	1	1	-1	1
INDONESIA R&H	**0**	**1**	**0**	**1**	**-5**	**-3**
MALAYSIA	-1	-2	74	346	74	492
MEXICO	-2	42	103	472	148	763
MOROCCO	0	0	0	0	0	1
PAKISTAN	0	0	0	0	0	0
PERU	0	2	0	1	0	3
PHILIPPINES R&H	-4	-3	-8	35	-9	10
SOUTH AFRICA R&H	7	196	322	672	1,048	2,245
THAILAND R&H	21	3,416	4,723	1,285	414	9,858
TUNISIA	0	0	0	1	0	1
URUGUAY	0	0	0	0	0	1
VENEZUELA	0	8	16	14	2	40
Total	11	3,827	5,555	3,154	1,611	14,158

n.a.: no data available. R&H: Retail & Hospital sales. Otherwise, retail sales only. French West Africa comprises Benin, Cameroon, Democratic Republic of Congo, Ivory Coast, Gabon, Guinea and Senegal. Central America includes Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua and Panama. Bold type indicates that the predicted change in the annual treatment doses is negative when switching to all drugs to no patent regime.

Source: Authors' calculations based on table 6 estimates.

Table 10.- Effect of the patent regime on availability

	Availability under no-patent regime	Availability under patent regime	Patent Effect:	
	Mean Pr(a=1|r=0)	Mean Pr(a=1|r=1)	Mean Pr(a=1|r=0) - Pr(a=1|r=1)	Number of ob.
ARGENTINA	0.62	0.56	0.06	56
BANGLADESH	0.04	0.14	-0.09	56
BRAZIL	0.43	0.44	-0.01	56
CENTRAL AMERICA	**0.20**	**0.29**	**-0.09**	**56**
CHILE	0.51	0.49	0.02	56
COLOMBIA	0.36	0.40	-0.04	56
DOMINICAN REPUBLIC	0.19	0.28	-0.09	56
EGYPT	0.06	0.16	-0.10	56
EQUADOR	**0.13**	**0.23**	**-0.10**	**56**
FRENCH WEST AFRICA	**0.06**	**0.15**	**-0.10**	**56**
INDIA	0.09	0.20	-0.11	41
INDONESIA R&H	**0.14**	**0.24**	**-0.10**	**56**
MALAYSIA	0.44	0.45	-0.01	56
MEXICO	0.43	0.44	-0.01	56
MOROCCO	0.11	0.22	-0.10	56
PAKISTAN	0.04	0.13	-0.09	56
PERU	0.17	0.27	-0.10	56
PHILIPPINES R&H	0.31	0.36	-0.06	56
SOUTH AFRICA R&H	0.77	0.67	0.10	56
THAILAND R&H	0.41	0.43	-0.02	56
TUNISIA	0.21	0.30	-0.09	56
URUGUAY	0.36	0.40	-0.04	56
VENEZUELA	0.24	0.32	-0.08	56
Total	0.28	0.33	-0.05	1,273

R&H: Retail & Hospital sales. Otherwise, retail sales only. French West Africa comprises Benin, Cameroon, Democratic Republic of Congo, Ivory Coast, Gabon, Guinea and Senegal. Central America includes Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua and Panama. Bold type indicates that the predicted change in the annual treatment doses is negative when switching to all drugs to no patent regime.

Source: Authors' calculations based on table 6 estimates.