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Patents and Pharmaceutical Drugs

Understanding the Pressures on Developing Countries

Julio Nogués

Lengthen effective patent protection in industrial countries and press developing countries to introduce patent protection. These two tactics have become important parts of the R&D-intensive pharmaceutical industry's strategy to regain losses in market share associated with more stringent drug safety regulations and increased competition from generic drug companies.

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This paper — a product of the International Trade Division, International Economics Department — is part of a larger effort in PRE to understand the economic impact of intellectual property rights. Copies are available free from the World Bank, 1818 H Street NW, Washington, DC 20433. Please contact Maria Teresa Sanchez, room S8-040, extension 33731 (41 pages).

For legal and economic reasons, patents allow drug-inventive companies to appropriate the returns from their innovations. Patents sustain high monopoly prices that provide rents to undertake further R&D and allow the invention of new drugs.

Much of the developing world — with very poor innovative capabilities — provide weak or no patent protection for pharmaceutical drugs. Moreover, some countries have not signed international patent agreements, and they provide no enforcement or dispute settlement mechanisms. To confront this situation, industrial countries have resorted to bilateral and multilateral pressures. For example, industrial country negotiators at the Uruguay Round (especially Japan, the EC, and the United States) have proposed that patents be offered in all fields (including pharmaceuticals), that they last 20 years from date of application, that compulsory licenses be applied only in extraordinary circumstances, and that a strong dispute settlement mechanism be established. By historical standards, these homogeneous proposals are unique. In general, developing countries have opposed these reforms. Some of them, such as Brazil and India, have done so explicitly.

Nogués indicates that the R&D-intensive pharmaceutical industry is one of few for which patents are a major instrument for protecting the returns from innovations. In this industry, investment in R&D is comparatively high, and drugs are easily copied. Under these circumstances, the legal protection of patents is of crucial importance in determining the market performance of the R&D-intensive pharmaceutical industry.

Stringent regulations introduced in the 1960s — to protect consumers from risky drugs — increased the costs of R&D in the U.S. pharmaceutical industry and reduced effective patent life (because the time needed on testing for complying with drug safety regulations has increased quite significantly). This reduces the profits per dollar invested in R&D. Also during the 1980s, several institutional changes seeking to reduce medical costs facilitated competition from generic drugs and squeezed the sales of the R&D-intensive industry. Finally, the potential market for patented drugs in developing countries is no longer trivial.

So this powerful industry is lobbying strongly for longer patent protection domestically and stronger protection in developing countries.

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PATENTS AND PHARMACEUTICAL DRUGS: UNDERSTANDING THE PRESSURES ON DEVELOPING COUNTRIES

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PATENTS AND PHARMACEUTICAL DRUGS: UNDERSTANDING THE PRESSURES ON DEVELOPING COUNTRIES [1]

Julio Nogués

I. Introduction

On September 1989--the deadline for a U.S. investigation --Argentina announced that within two years it would submit a draft law extending patent protection to pharmaceutical products. One year earlier--on October 20, 1988--the U.S. Federal Register published the list of goods on which the U.S. would retaliate by increasing ad-valorem tariffs rates to 100 percent on imports from Brazil; this country had refused to negotiate patent protection to pharmaceutical drugs. On December 18, 1987, the EC removed Korea from the list of countries eligible for GSP treatment. The reason: Korea had refused to grant EC manufacturers the same intellectual property protection it affords to U.S. exporters. The EC, Japan and the U.S. have all tabled proposals at the Uruguay Round for significantly greater homogeneity and higher protection of Intellectual Property Rights (IPRs)--patent protection to pharmaceuticals probably being the most significant item in this agenda--around the world. The proposals are directed at developing countries, which--so far--have resisted

This list--which goes on--of bilateral and multilateral actions raises a question: why all these pressures on developing countries? The

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[1] I appreciate comments received from Bela Balassa and Paul Meo. I also appreciate efficient typing from Maria Teresa Sanchez.

hypothesis of this paper is that part of these pressures evolve as a reaction to institutional and competitive changes that have taken place in the pharmaceutical drug markets of industrial countries. Most importantly, these changes refer to tighter drug safety and efficacy regulations and to increased competition from generic drugs. At the same time, besides patents other policies of developing countries -- such as trade barriers, price controls and, (most importantly) the administration of regulations--also have an impact on competitive positions of different firms. Nevertheless, this paper focuses on developments taking place in industrial countries.

The plan of the paper is as follows: Section II will review the worldwide pattern of patent policies and the pressures from industrial countries on developing countries for modification of patent laws in general, and pharmaceutical drugs in particular. Section III presents the evidence on the relative importance of patents for the pharmaceutical industry. Section IV discusses changes in effective patent duration as modified by regulatory policies. Section V presents evidence on the growing importance of competition between brand names and the generic drug industry and the impact of this competition on drug prices. Section VI presents some final remarks.

II. Pressures on Developing Countries

The purpose of this section is to highlight the pressures put by industrial countries for reforming patent policies in LDCs. It first presents the worldwide pattern of patent protection for pharmaceutical drugs and the proposals for reform of patent policies tabled at the multilateral trade negotiations of the Uruguay Round. Subsection 1 will also argue that for the first time in modern economic history, industrial countries have come to an

agreement on "appropriate" patent protection. Subsection 2 will provide a brief discussion of some of the bilateral actions taken by industrial countries against developing countries; the existing patent policies of many of these countries are quite apart from the proposals of industrial countries. Finally, subsection 3 will provide a brief discussion of the economic interests at stake.

1. Patent protection to pharmaceuticals

While today a great majority of industrial countries provide patent protection for pharmaceutical drugs, there are many developing countries that do not. Nevertheless, it should not be concluded that patent protection for pharmaceuticals has a long tradition in industrial countries. For example, only in 1949 did the United Kingdom introduce patent protection for pharmaceutical drugs. Also, many other industrial countries have only recently introduced patents for pharmaceuticals, including Germany, 1968; France, 1960; Italy, 1978; Japan, 1976; Sweden, 1978; and Switzerland, 1977. Thus, among industrial countries, for many years the pharmaceutical industry was one of a few that remained unprotected by patents. Even today some industrial countries such as Australia, Finland, New Zealand and Norway, still refuse to grant patent protection to pharmaceuticals; Spain will introduce it only in 1992 (Lobo, 1988).

Furthermore, at different times, industrial countries enforce a system of patent licenses that restricts the monopoly of the patent owner quite significantly. This is the case, for example, in Canada and the United Kingdom. Other countries--including the U.S.--have used antitrust legislation to control license agreements. For example, when discussing the patent system in general, Scherer asserts that "...compulsory licensing has been specified as a remedy in

more than 100 antitrust cases, making available some 40,000 to 50,000 patents at 'reasonable' royalties or (in a few instances) royalty free ..." (Scherer, 1980, p. 397).

On the other hand, many developing countries have not yet introduced patent protection for pharmaceuticals. As a matter of fact, the pharmaceutical industry is the one most often excluded from patent protection in developing countries.[2] The World Intellectual Property Organization (WIPO, 1988), has listed 49 countries as not providing patent protection for pharmaceutical products:[3] Argentina, Australia*, Bolivia, Brazil*, Bulgaria, Chad, China, Colombia*, Cuba, Czechoslovakia, Ecuador, Egypt, Finland, Germany Democratic Republic, Ghana, Greece, Hungary, Iceland, India, Iran, Iraq, Korea, Lebanon, Libya, Malawi*, Mexico*, Monaco, Mongolia, Morocco, New Zealand*, Norway, Pakistan, Peru, Poland, Portugal, Romania, Soviet Union, Spain (until 1992), Syria, Thailand, Tunisia, Turkey, Uruguay, Venezuela, Vietnam, Yugoslavia, Zambia* and Zimbabwe*.

As seen from the above list, there are many countries that provide patent protection for pharmaceutical processes, but not pharmaceutical products. A process patent protects the product only if it is produced with it. Since small modifications of a formula create many ways of producing a chemical compound, process patents are generally viewed as providing weak protection for

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[2] Other products and/or processes that are quite often excluded from patent protection are animal varieties, methods for treatment of human or animal body, plant varieties, biological processes for producing animal or plant varieties, food products and computer programs (WIPO, 1989).

[3] An asterisk indicates that patents for pharmaceutical processes are also excluded.

pharmaceutical drug companies. Furthermore, in developing countries the courts have often interpreted the exclusion of pharmaceutical product patents as a policy for enhancing competition in the drug market. Thus, when cases of process patents have been brought to trial, the courts have usually turned down demands to use these patents to protect the monopoly power of the product.

Thus, a significant part of the developing world, provides weak patent protection for pharmaceutical drugs; very often patent protection is not provided or, if provided, it is not legally strong. This situation has become an issue for multilateral negotiations between developed and developing countries. Also, the lack of patent protection for pharmaceutical drugs has triggered numerous bilateral actions of industrial against developing countries. According to Benko (1988), these complaints refer to the characteristics of both the international and domestic patent regimes. Industrial countries argue that the international patent regime is inadequate because a number of countries have not signed some of the international agreements and also because they provide no enforcement or dispute settlement mechanisms. Furthermore, industrial countries complain that domestic patent regimes of many developing countries are inadequate because patent protection: is too short; some industries such as pharmaceuticals are excluded; the legal enforcement of patent rights is weak; and too much emphasis is given to compulsory licensing.

At the Uruguay Round, industrial country negotiators --including those of the EC, Japan and the US -- have proposed among other things that patents should be offered in all fields; that they should last for 20 years from date of application; that compulsory licenses should be applied only in extraordinary circumstances and that there should be a strong dispute settlement mechanism. The few developing countries that have tabled proposals on

intellectual property rights -- for example Brazil and India -- oppose these reforms. The only exception is Korea, which has tabled a proposal very similar to that of industrial countries.

Thus, we might conclude that from an historical perspective the current situation finds industrial countries in quite general agreement on a policy issue -- patent protection in general and for pharmaceutical drugs in particular -- where until not long ago important differences were observed among them. Explaining this is not easy, but at the very least we can say that neither theory nor empirical research provide support for the current state of affairs. There is no theory of patents powerful enough to provide those in favor of the above mentioned patent policies with strong support (Braga, Evenson and Lesser, 1990). The most general economic model of patents is that of Nordhaus (1969); in this model it is only under a very particular set of parameter values that the industrial countries' proposals can be defended.[4]

On the other hand, empirical research has shown that social returns to R&D are quite high and generally higher than private returns (Mansfield, 1977); this evidence is used to support patent. Furthermore, the evidence is only for industrial countries; research on the social rate of return of drug innovation in developing countries has not been undertaken and the reason appears to be simply that these countries do not undertake drug research.

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[4] This particular set of parameter values includes the productivity of R&D which is expected to differ quite significantly among industries and countries.

2. Bilateral policies and actions

In March of 1987, only a few months after the Uruguay Round had been launched, Mr. Gerald J. Mossinghoff, President of the U.S. Pharmaceutical Manufacturers Association (PMA) declared that they were working with the U.S. Congress to get it to enact "...the intellectual property revisions of the Omnibus Trade bill that would strengthen the hand of the U.S. Government in urging all of our trading partners to respect our rights in inventions and trademarks..." (PMA, 1987, underlined by the author). Shortly after, the U.S. Omnibus Trade Act of 1988 was passed, modifying the administrative provisions of bilateral trade instruments. The most significant changes for the pharmaceutical industry were introduced to Section 301 of the Trade Act of 1974 (henceforth Section 301). This Section provides for the enforcement of U.S. rights under international trade agreements and for the relief from "... unfair practices of foreign governments which can be unjustifiable, unreasonable, discriminating or which burden or restrict U.S. commerce."

If in a Section 301 investigation the foreign country is found to be "violating" U.S. rights and it does not correct its policies, the United States Trade Representative (USTR) --in charge of the 301 investigations-- can recommend the use of retaliatory measures. The Omnibus Trade Act introduced important changes to Section 301; changes which, according to Grinols (1988), would make it easier for the U.S. to expand the number of 301 cases, increase the likelihood of finding the investigated country was acting unfairly, and most likely increase the magnitude and duration of the retaliatory measures.

Also, among the changes introduced, is a mandate for the USTR to identify priority countries that deny adequate and effective protection of intellectual property rights; currently India is on this USTR list. The U.S.

has threatened to use Section 301 in more cases than those actually investigated. For example, under strong pressures, Korea passed legislation in 1986 that would allow patent protection for pharmaceutical products (Gadbaw, 1988). However, the attack on Korea's patent policies did not come only from the U.S. In December 1987, the EC removed Korea from the GSP because it did not provide adequate patent protection for the R&D intensive pharmaceutical industry (WIPR, 1988).

Under similar pressures, other countries have announced that they will introduce patent protection for pharmaceutical products; e.g., Mexico (Gwyn, 1988) and Argentina (Nogués, 1990). But retaliatory threats have not always ended with positive changes by developing countries. Probably, the most notorious case has been the retaliatory action against Brazil undertaken after completion of a 301 investigation. Among other things, this investigation -- initiated by the PMA -- estimated the injury to U.S. firms because of absence of patent protection for pharmaceutical processes and products. Because Brazil did not satisfy the demands by the PMA, the U.S. increased ad valorem tariff rates to 100% on an important number of goods imported from Brazil (U.S. Federal Register, October 24, 1988).[5]

It is quite clear from all this that developing countries have confronted, and continue to confront, significant pressures from industrial countries in order for them to introduce patent protection for pharmaceutical

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[5] Brazil used to be in the USTR watch list, but was deleted in 1990 for having made progress in a number of issues; trade liberalization policies were an important factor. On July 2, 1990 this progress also led the U.S. to lift the retaliatory tariff of the 301 pharmaceutical case. Finally it should be said that Brazil challenged this U.S. 301 action in a GATT dispute settlement panel.

products. The choices for developing countries have narrowed; either they increase protection to intellectural property and in particular extend patent protection to pharmaceutical drugs, or otherwise suffer actual or threatened retaliatory actions by industrial countries.

3. The economic interests at stake: a preliminary discussion

What would the pharmaceutical companies of industrial countries gain from the introduction of patent protection in developing countries? How important are these gains? The first question is easy to answer, but the second has only recently begun to be analyzed. Essentially, introduction of patent protection would put an end to the era of copying brand name pharmaceutical drugs by domestic companies of developing countries. After patent protection is introduced, only brand name companies will be the "legal" suppliers of patented drugs.

Regarding the importance of the pharmaceutical drug market and the loss to copiers, the PMA has made estimates of some countries, these are presented in Table 1. Part of the pharmaceutical drug market in these countries is supplied by patent owners, but part is also supplied by copiers; the proportion supplied by these latter type of firms varies between countries, being highest in India (36.1%) and lowest in Brazil (5.5%).[6] Overall, in these four countries, the PMA estimates that the sale of copied drugs amounts to US$1.4 billion per year. The speed at which domestic copiers would loose their market to patent owners depends in part on whether patent protection would be enforced

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[6] These proportions have varied quite drastically over time as economic conditions and regulatory behavior have come to benefit multinational companies or domestic companies. See for example Katz and Groisman (1988) for the case of Argentina.

retroactively. In the absence of retroactive enforcement, the rate of market loss of copiers will depend in part on the rate of introduction of new patented drugs.

Table 1: ESTIMATES OF INCREASED INCOME OF PHARMACEUTICAL COMPANIES HOLDING PATENTS (US$ M)

Variables \ Countries	Argentina	Brazil	India	Mexico	Total
1. Pharmaceutical market size	1,200.0	2,000.0	4,200.0	1,000.0	8,400.0
2. Patented pharmaceutical market	771.0	1,750.4	2,546.0	852.5	5,919.9
2.1 Sales by domestic firms of copied drugs	231.0	93.8	920.0	136.5	1,381.3
2.2 Sales of drugs by firms who are patent owners	540.0	1,656.6	1,626.0	716.0	4,538.6
3. Percentage share of U.S. companies a/	45.0	50.0	45.0	50.0	n.a.

a/ Refers to share of sales of U.S. companies in total sales by multinationals.

Source: Mac Laughlin, et. al. (1988).

The US$1.4 billion is a fraction of the worldwide sales of R&D intensive pharmaceutical companies; it is likely that this fraction has increased. This is certainly one of the reasons why the pharmaceutical drug

companies are pressuring developing countries. But the central hypothesis of this paper is that these pressures are also triggered by changes which have occurred in industrial countries. The R&D intensive industry seeks to maintain and regain the market share that has been increasingly lost to the generic drug industry. A major component for achieving this goal is to increase patent protection.

III. The Importance of Patents to the Pharmaceutical Drug Industry

This section makes three points. First, patents are important, but only to a few industries, one of which is pharmaceutical drugs (Subsection 1). Second, the importance of patent protection for this industry comes from the strength that they provide in litigations (Subsection 2). Finally, although patent protection is important to only a few industries, the pharmaceutical drug industry happens to be among the most R&D intensive and as a matter of fact, invests an important proportion of aggregate R&D.

1. The inter-industry importance of patents

There is a general presumption that patents are an important instrument for allowing inventors to appropriate the returns from inventions. In evidence accumulating in recent years shows that patents are far more important for some inventions and industries than for others. Probably the pioneering study to throw light on this issue was undertaken by Mansfield (1986). His figures are reproduced in Table 2; they show by industry and for the early 80's, the percent of inventions that would not be developed nor introduced into the market in the absence of patent protection. According to these figures, far more of the innovations produced by the pharmaceutical drug industry would

not had been developed or introduced in the absence of patent protection.

Mansfield's conclusions received important support from a comprehensive study undertaken by Levin, et. al (1987). This study examined

Table 2 : PERCENT OF INVENTIONS THAT WOULD NOT HAVE BEEN DEVELOPED OR INTRODUCED IN THE ABSENCE OF PATENT PROTECTION a/

	Percent that would not have been introduced	Percent that would not have been developed
Pharmaceuticals	65	60
Chemicals	30	38
Petroleum	18	25
Machinery	15	17
Fabricated Metal Products	12	12
Primary metals	8	1
Electrical equipment	4	11
Instruments	1	1
Office equipment	0	0
Motor vehicles	0	0
Rubber	0	0
Textiles	0	0

a/ Some inventions that were developed in this time period (1981-83) were not introduced then, and some inventions that were introduced then were not developed then. Thus, the left-hand column of the table refers to somewhat different inventions than does the right-hand column.

Source : Mansfield (1986)

the relative importance of different ways of protecting the inventor's returns on his inventions. The authors prepared a comprehensive questionnaire and interviewed research managers from 130 U.S. industries. One set of questions included the views of these managers regarding the importance of alternative means of appropriating the returns from the innovations made by their enterprises -- patents to prevent duplication, patents to secure royalties, industrial

secrets, lead time, learning advantages and sales and/or service efforts. The authors distinguished between process and product innovations and the answers were rated on a one to seven scale. The study showed that on average the most important means of appropriating the returns in process and product innovations are lead time and sales/service efforts; in contrast, patents to secure royalty income in process and product innovations were only 65% and 67% as important as lead time and sales-service efforts respectively.

Table 3 from Levin, et. al. (1987) answers a similar question to that raised in Mansfield (1986), namely what is the inter-industry importance of

Table 3: EFFECTIVENESS OF PROCESS AND PRODUCT PATENTS AS A MEANS OF PROTECTING THE RETURNS FROM INDUSTRIAL INNOVATION

Industry	Process Patents	Product Patents
Pulp, Paper and Paperboard	2.6	3.3
Cosmetics	2.9	4.1
Inorganic chemicals	4.6	5.2
Organic chemicals	4.1	6.1
Drugs	4.9	6.5
Plastic materials	4.6	5.4
Plastic products	3.2	4.9
Petroleum refining	4.9	4.3
Steel mill Products	3.5	5.1
Pumps and pumping equipment	3.2	4.4
Motors, generators and controls	2.7	3.5
Computers	3.3	3.4
Communications equipment	3.1	3.6
Semiconductors	3.2	4.5
Motor vehicle parts	3.7	4.5
Aircraft and parts	3.1	3.8
Measuring devices	3.6	3.9
Medical instruments	3.2	4.7
Full sample	3.5	4.3

Source: Levin, et. al., (1987).

patents for appropriating the returns from innovation. Again the answers are rated on a one to seven scale. The figures in this table show that patents are most important to protect the process and product innovations of the drug industry; these patents were rated 40% and 51% higher than the industrial industrial averages for processes and products respectively. Furthermore, "... only five of 130 industries rated product patents to prevent duplication higher than six (out of seven) points ..." (Levin, et. al. , 1987, p. 795). Drugs were one of the five.

The importance of patents for the pharmaceutical drug industry is not restricted to the U.S. For example, in a classic study of the British patent system, Taylor and Silberston assert that the "... pharmaceutical industry stands alone in the extent of its involvement with the patent system ..." (Taylor and Silberston, 1973, p. 231). Clearly then, in industrial countries patents are a crucial policy instrument in determining the returns to innovative efforts in a core group of industries and particularly for pharmaceutical drugs.

2. The inter-industry strength of legal protection

There are several hypotheses as to why the importance of patents differs so markedly between industries. For example, in some industries such as consumer electronics the rate of innovation and product differentiation is so fast that lead times are the most natural way of appropriating the returns from innovation. On the other hand, many innovations may not be patentable in the sense of satisfying the requirements for a patent; namely, that the invention is novel, that it has utility and that it is non-obvious. But even if an invention were patentable, it could be that because a patent discloses

valuable information, the owner would prefer to keep it as a secret. This could be particularly important when the inventor fears that the courts will not protect his patent rights.

Precisely this legal aspect is an important factor that explains the importance of patents to the pharmaceutical industry; to quote, the "... most probable explanation for the robust finding that patents are particularly effective in chemical industries is that comparatively clear standards can be applied to assess a chemical patent's validity and to defend against infringement. The uniqueness of a specific molecule is more easily demonstrated than the novelty of, for example, a new component of a complex electrical or mechanical system. Similarly, it is easy to determine whether an allegedly infringing molecule is physically identical to a patented molecule; it is more difficult to determine whether comparable component of two complex systems do the same work in substantially the same way." (Levin, et. al., p. 798). This quote could also be extended to pharmaceutical drugs for which as said, patents are the most important means of appropriating the returns from R&D.

3. The relative importance of R&D invested by the private pharmaceutical industry

The amount of R&D undertaken by the private pharmaceutical drug industry is very high. First, firms in this industry typically invest a minimum of around 10% of their sales in R&D. But in some countries like the U.S., this proportion increased during the 1980s and--according to the PMA--reached 16% in 1988. This contrasts with the economy-wide average R&D investment as a proportion of GDP of industrial countries which stands at around 2.5% (Evenson, 1990). This puts the pharmaceutical firms among the most intensive R&D

industries of industrial countries. Second, these firms are generally huge; in 1982 each of the thirty largest pharmaceutical drug companies of the world had sales above US$1 billion. Third, in absolute terms, the total amount of R&D invested by pharmaceutical firms in industrial countries is enormous. For example, according to PMA reports, investment in R&D of the private U.S. pharmaceutical firms exceeds US$7 billion; the industry is proud to remind the general public that this is higher than the total investment undertaken by the U.S. National Institute of Health for biomedical research (emphasized by the PMA in the Washington Post, November 17, 1989, p. A60). Such a figure also represents close to 10% of all U.S. R&D investment.[7]

Summing up, in only a few industries do patents appear to be a major instrument for fostering technological innovation and diffusion; in the great majority, innovation appears to be triggered by market conditions. One of the few industries where patents are a major instrument for protecting intellectual property is pharmaceutical drugs. Although these drugs are easily copied--with or without the information disclosed in the patent (Mansfield, 1985)--they are unique innovations and therefore, the legal protection provided by patent litigation is clearly in favor of innovating firms. Finally, although for many industries patents are generally unimportant as a means of appropriating the returns from R&D, given the size of R&D invested by the private U.S. pharmaceutical drug companies, one may conclude that patents are an important instrument in protecting a non-negligible portion of the output of total R&D of industrial countries.

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[7] Among the 30 largest pharmaceutical companies, 14 are from the U.S., 12 are European and four from Japan (The Financial Times, 4/11/89, p. 23).

IV. Safety Regulations, Productivity of R&D and Effective Patent Duration: The Case of the U.S.[8]

This section makes essentially two points. First, there are two approaches to deal with the fact that pharmaceutical drugs can be a source of serious health risks; these approaches can be biased towards the market mechanism or towards a governmental enforced regulatory system. The history of the U.S.--and other industrial countries--shows a clear drift towards the second approach (Subsection 1). Second, the stringent regulations introduced in the U.S. during the early 1960s, has had clear effects on the costs and productivity of R&D undertaken by private pharmaceutical companies. Furthermore, increased safety and efficacy regulations have reduced the effective patent protection, thus reducing the profits per dollar invested in R&D (Subsection 2). This has been an important argument in defending this industry's request for longer patent duration; it is also a factor in explaining the industry's demand for higher protection in developing countries.

1. Market induced information flows vs. government safety regulations

The purpose of this section is to discuss the effects of the changing regulatory environment of pharmaceutical drugs in the United States. Safety regulations in the area of these drugs are justified with the argument of market failure. The problem is that pharmaceutical drugs can be a source of serious risks; in fact, some fatal cases associated with their consumption have shaped

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[8] This section draws from Grabowski and Vernon (1983).

the nature of regulations in the U.S. as well as in other countries. The problem is essentially one of incomplete and/or inaccurate information which is more serious in the case of new and relatively undertested drugs. The solution, or at least the reduction in health risks, lies in improved information on positive and negative effects of drugs.

Two ways to reduce health risks can be envisaged; market-oriented and government-oriented. In a market-oriented approach, the quality and quantity of information on drug therapy would rely mainly on the quality of the doctors and the professional management of manufacturing enterprises. Presumably, the degree of market success of these agents would be linked to their professionalism. Furthermore, potentially abusive behavior by these agents would be checked by other institutions; the law would define the boundaries under which behavior by doctors and firms could remain unpunished. The Government could also reinforce the market by directly providing or enticing private parties to improve and disclose the best information possible.

An alternative approach would suggest that because the market is unreliable for these purposes, it is preferable to introduce a centralized regulatory agency. This alternative course of action is likely to be taken when the perceived risks of relying on the market remains very high. The U.S. pharmaceutical drug history demonstrates this latter approach; today the U.S. Government shares major responsibility for negative health consequences that could arise from the marketing of risky drugs. The first law regulating pharmaceuticals was the Pure Food and Drug Act of 1906. This law prohibited adulteration and mislabelling of food and drugs. The aim of the law was to improve the quality of information, and the role of government was essentially

to prosecute violators and, when necessary, withdraw their products from the market.

In 1938, the Food, Drug and Cosmetic Act tightened regulations of pharmaceutical drugs. The law was passed after several hundred children died as a consequence of the combination of sulfanilamide and the poisonous diethylene glycol, which had been marketed without toxicity tests. The new law required firms to submit a new drug application (NDA) to the Food and Drug Administration (FDA), demonstrating that the drug was safe. The application was automatically approved in sixty days unless the FDA recommended otherwise. These regulations remained unchanged until 1962.

In spite of the tighter regulations between 1938 and 1962, R&D continued to increase and during those years major medical discoveries--particularly in the area of antibiotics--were introduced. In fact, in terms of profits, the pharmaceutical industry was one of the best performers. The perfo nance was so visible that in the early 1960s, Senator Estes Kefauver begun a series of congressional hearings with the aim of reducing the market abuses of pharmaceutical drug companies which were claimed to be associated with patent rights. Senator Kefauver advocated the introduction of compulsory licensing. At the same time, the thalidomide case occurred, and the nature of the discussions on the pharmaceutical industry shifted from one of market abuses to one of product safety. In 1962 the Kefauver-Harris Amendment to the Food, Drug and Cosmetic Act of 1938 was passed. The major provisions of the amendment include a requirement of efficacy and the establishment of FDA regulatory controls. Furthermore, the provision to approve a new drug application within 60 days was repealed; the FDA is now quite free to take whatever time is

necessary for approving a drug.[9]

2. Consequences of the 1962 drug safety regulations

The new regulations have made the U.S. Government switch from a role of legislating for improving market performance to one of regulating directly via the FDA. As a consequence, the duration and stringency of the tests that the FDA requires for approving new drugs increased considerably. The average industrial phase of testing for toxicology and effectiveness is estimated to be 6.4 years. It is only after 2 to 15 volumes of material and 10 to 100 volumes of raw data that the firm is ready to submit to the FDA an application for approval.

In 1963, the average time it took the FDA to decide on a new drug was fourteen months. By 1979, the average time had increased to thirty five months and in 1986 it was thirty seven months. As a consequence of the increased and lengthier tests, the average time to develop a new drug from start to market is around 10 years--a major factor in reducing effective patent protection--and the average cost per approved pharmaceutical drug has increased to US$125 million.[10] This cost includes those associated with all (successful and unsuccessful) new chemical entities that enter clinical testing.

The regulations also had severe consequences on the productivity of R&D. For example, after 1962, the number of new drugs marketed in the U.S.

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[9] The thalidomide case had worldwide implications on the nature of regulations for drugs. For a discussion of the changes introduced in the U.K. see Hartley, et. al, (1986). But in spite of these changes, the U.S. regulations are believed to be among the most stringent in the world.

[10] Estimated by the Pharmaceutical Manufacturers Association (The Washington Post, November 17, 1989 p. A-60).

declined from around 50 per year to 20 in 1986. Some observers have attributed this decline to the depletion of research opportunities, but the bulk of the evidence suggests that this was primarily associated with the 1962 regulations. This is borne out not only by time series analysis of the U.S. but also by cross-section analysis.

The consumer loss from lower drug innovations as well as the fact that even approved drugs are introduced with an important lag in relation to other countries can be substantial. The counterpart benefits of the new drug regulations have apparently been small. For example, Peltzman (1975) has estimated that the cost of avoiding the introduction of ineffective drugs could be four times higher than the benefits that would accrue if more and faster introduction of drugs were allowed.

The question has also been looked at in an international perspective by comparing the U.S. with Europe, which has less stringent regulations. Perhaps because of this, between 1964 and 1975, Europe discontinued the marketing of five drugs. The benefits for the U.S. of not having introduced these drugs--because Europe learned before of the risks--has not been estimated, but there is agreement that these benefits probably have been small.[11] An indicative and serious case, in terms of health consequences in the U.S., was Zomax, a prescription painkiller. After more than two years this product was withdrawn from the U.S. market in early 1983 when reports showed that severe allergy reactions could occur. Later in 1985, a study by the FDA concluded that Zomax

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[11] There has also been a case of a new drug--Oraflex--that was introduced into the U.S. market and later discontinued, when in Europe--where the drug had been introduced before--it was noticed that in some cases it had severe side effects.

had probably been a factor in 14 deaths and in 403 life-threatening reactions. This case led to numerous litigations against Mc Neil Pharmaceutical, a subsidiary of Johnson & Johnson, and the producer of Zomax (Washington Post, October 25, 1988). The conclusion from this is that, in spite of heavy regulations, health risks continue to exist. There also is little evidence that the consumer benefits in the U.S. where regulations apparently are much stricter, are higher than in other countries.

Finally, it could be argued that more stringent regulations have reduced the number of ineffective drugs being introduced into the market. While this might be true, it appears that the proportion of ineffective to total new drugs did not decline after 1962.[12]

In summary, the evidence for the U.S. shows that increased regulations have had a clear impact on the average time it takes from the moment when research on a new chemical compound starts until the moment when the FDA approves the new drug for marketing.[13] This has reduced the effective patent protection and today, the protection is much shorter for the pharmaceutical industry than it is for other industries. In addition, several institutional changes introduced during the 1980s have facilitated competition from generic drugs. This, plus the fact that patents are a powerful instrument for sustaining drug prices, implies that the rate of profit per dollar of R&D must have declined

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12 An alternative hypothesis--suggested to me by Jorge Katz,--is that the increased regulations and testing could have provided a further source of learning from which the industry and the population at large has benefitted. To my knowledge, the importance of this hypothesis remains unknown.

13 There are also reports arguing that a similar trend has occurred in the EC. See for example Hartley, et. al., (1986).

with the extent of generic drug competition. I now turn to a discussion of the impact of generic drug competition on drug prices.

V. Increasing Competition from Generic Drugs

During the 1980s, there have been a number of policy changes which have facilitated competition from generic drug companies in the United States. Subsection 1 reviews some of these policies, and subsection 2 reviews the impact of generic drug competition on prices.

1. Institutional changes and generic drug competition

Traditionally, the R&D intensive pharmaceutical firms could count on a number of institutions for lengthening the impact of patent protection after their expiration. First, anti-substitution laws meant the pharmacist could sell to customers only the brand prescribed by the physician. These laws in effect extended the effective patent life beyond the legal life. In fact, the first entrant into a new drug market had a privilege that in some cases extended the monopoly position well beyond the statutory patent duration (Gorecki, 1986; Comanor, 1986; McRae, et.al., 1985). This situation was facilitated by misinformation or underinformation to the consumer, who takes decisions based fundamentally on what his/her physician and pharmacist recommend (Hall, 1986). Such recommendations can overcome important price differentials which usually develop between brand names and generic drugs.

The 1984 Patent Restoration Act--to be discussed below--which facilitated the introduction of generic drugs, came at around the same time that other institutional changes were being introduced. First, the elimination of anti-substitution laws in practically all U.S. states, permitted the pharmacist

to suggest to the client the existence of a generic equivalent to the prescribed drug. The consumer choice can only be avoided when the physician explicitly prescribes that the patient should consume a drug from a specific company.

Other U.S. policies which foster the consumption of generics are cost containment policies, such as limited reimbursement lists. Also, Medicaid programs and even private insurance companies are recommending the use of generics. All this implies that, in general, once patent protection expires, competition from the generic producing companies becomes important as soon as the FDA approves these drugs for marketing; in fact, as we shall see, the 1984 Patent Act reduced FDA regulations for generic drug approval. To quote "... The experience of two leading pharmaceuticals, Valium and Inderal, that have experienced generic competition for the first time this year illustrates these trends. These two drugs have lost approximately one quarter of their respective market shares on new prescriptions to generic products selling at price discounts of 20 percent or more. This has occurred within the first three months of generic availability. Another leading pharmaceutical, Indocin, has lost approximately half its market share in only its second year of generic competition. These rates of sales' losses are far in excess of historical patterns in pharmaceuticals, or what was experienced only a few years ago..." (Grabowski and Vernon, 1986).

The extent of competition from generic drugs is apparently much more important than what these two cases show. For example, the combined U.S. market share of the 13 widely prescribed generic drugs has increased during the 1980s

from around 30% to 60% of total drug sales.[14] This trend is expected to increase as patents on major selling drugs expire in the early 1990s.

The R&D intensive pharmaceutical firms can overcome this competition by increasing patent duration and/or by becoming more productive, i.e., by introducing drugs in the market at a faster rate. The figures show that the productivity of R&D continues to remain stagnant. For example, according to reports by the PMA, between 1984--when effective patent duration was extended--and 1989, R&D by the U.S. pharmaceutical industry increased from a little less than US$4 billion, to US$7.3 billion. In spite of this, for years the trend in the annual number of new drugs approved by the FDA, has not changed significantly.[15] In part, this should be attributed to the lag between initial research and final FDA approval. If the productivity of R&D in the drug industry continues to remain stable, competition from the generic drug industry will likely continue to increase. For example, it is estimated that the market of major drugs whose patents will expire during the 1990s is around US$10 billion and an important part of this market will be lost to generic drugs.[16]

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[14] The Wall Street Journal, "Generic Drug Scandal Creates Opening," September 6, 1989.

[15] For example, during the consecutive years between 1980 and 1989, the number of new drugs approved by the FDA was 12, 27, 28, 14, 22, 30, 20, 21, 20 and 23.

[16] The patents of the following major drugs will expire in the indicated year: Seldane (Dow Chemical, 1992); Tagamet (Smith Kline, 1994); Zantac (Glaxo/Sandoz, 1994); Pepcid (Merck, Johnson and Johnson, 2000); Naprosyn (Syntex/Procter & Gamble, 1993); Feldene (Pfizer, 1992); and Nicorette (Dow Chemical, 1992). (The Wall Street Journal, June 5, 1989, p. B1).

2. The Impact of Generic Competition on Drug Prices

Disentangling the role of patents on drug prices is a difficult task, particularly when other regulations--including price controls--are imposed. Furthermore, although patents provide a monopoly, prices will also reflect the extent of competition among different patented drugs in given therapeutic classes. In spite of the difficulties of analyzing the impact of patents on drug prices, two patterns tend to appear quite neatly. First, generic drug prices are well below brand name prices; also, an important share of the market is taken by generic drugs. Second, the price of drugs appears to be systematically lower in countries that do not provide patent protection for pharmaceuticals.

2.1. The impact of generics on drug prices

It has often been noticed that generic drugs enter the market at high discounts vis a vis the brand names. The extent of such price differentials is best studied in markets with free prices. In this regard, the U.S. is generally believed to have one of the freest pharmaceutical drug market in the world.[17] For example, Scherer (1980, p. 390) reports that for many years Pfizer sold the antibiotic Tetracycline at US$30.60 per 100 capsules. When Pfizer's patent was challenged, competing firms sold the generic product at US$2.50 per bottle. Furthermore, Scherer asserts that many "...similar cases of price cost-margins in the order of 90% for patented drug products have been identified..."

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[17] This does not mean that free pricing is always allowed. See, for example, a discussion of the debate on this issue published in The Washington Post of June 11, 1989 (p. H1) and the recent control on the AIDS drug AZT, by which the government brought down the annual cost of treatment from US$8,000 to US$6,000.

Other examples illustrate the impact of generic drug introduction. One hundred tablets of 2 mg. pills of Valium are wholesale priced at around US$30.- while the generic Diazepan sells for around US$15.- One hundred tablets of 600 mg pills of Motrin are wholesale priced at around US$25.- while the generic Ibuprofen is priced at around US$14.- Another example made by the President of the American Association of Retired Persons, asserts that its members pay US$15.95 for a 3 months supply of Bolar's version of Dyazide and US$31.95 for the Smith Kline brand name product. The same source asserted that there might be a 10 to 1 difference in the price of different arthritis drugs (The Wall Street Journal, September 6, 1989). Similar price differences are found in many other examples of drugs that have gone off patents such as Aldomet, Amixil, Inderal, etc.[18]

Finally, major reductions in drug prices after patent expiration have also been reported in other countries. For example, Taylor and Silberston report that "...U.K. price reductions of the order of a quarter to a half or more have been noted at this stage of the life-cycle of important patented drugs." (Taylor and Silberston, 1973).

In conclusion, over time patents appear to be a major factor in sustaining drug prices. Also, the appearance of generic competition is a significant factor in bringing these prices closer to marginal production costs

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[18] One might ask what explains the post-patent pricing strategy of brand name companies when they allow such significant price differentials with their competing generic drugs. One plausible explanation is that over their life brand name drugs create a clientele of relatively wealthy doctors and patients who in spite of low priced generic drugs, they prefer to remain loyal to the medicine they have been prescribing and taking.

(see also U.S. Congress, 1986); the market becomes more competitive, not perfectly competitive.

2.2 The cross-country evidence

Prices of pharmaceuticals also differ significantly among countries. Table 4 shows a cross-country comparison of an index of 1975 prices of identical

Table 4 : CROSS-COUNTRY PRICES INDEX OF PHARMACEUTICALS - 1975

Country	Price Index Pharmaceuticals	Country	Price Index Pharmaceuticals
Malawi	60.83+	Ireland+	73.58+
Kenya	50.63+	Hungary	57.25
India	31.71	Poland	53.98
Pakistan	38.76	Italy	69.01
Sri Lanka	15.22+	Spain	69.68
Zambia	96.58+	United Kingdom+	71.19+
Thailand	48.01	Japan	81.88
Philippines	51.14+	Austria	139.53
South Korea	35.10+	Netherlands+	137.29+
Malaysia	70.74	Belgium+	101.73+
Colombia	48.07	France+	91.56+
Jamaica	46.13+	Luxembourg+	100.27+
Brazil	63.83	Denmark+	157.56+
Mexico	69.68	Germany (F.R.)+	152.52+
Yugoslavia	48.24	United States+	100.00+
Iran	70.42	Uruguay	65.95

\+ Listed in Schut and Van Bergeijk (1986) as providing patent protection.

Source: Schut and Van Bergeijk (1986, Table 2). Patent information for 1988 from WIPO (1988).

packages of pharmaceutical products. After fitting a simple econometric model Schut and Van Bergeijk concluded that a "...strong positive relationship between price level and per capita GDP is found, a 10% increase in per capita income

being associated with on average 8% higher drug prices. The implementation of direct price control measures by the government results on average in a 20% price reduction, while government policies such as bulk purchasing through a centralized government agency, promotion of the use of generics and, to a lesser extent, excluding patent protection seem to be successful in lowering the general price level of pharmaceuticals." Schut & Van Bergeijk, 1986 p. 1141).[19]

Looking at the econometric results--according to which the patent dummy variable was not statistically significant--one might be tempted to conclude that in terms of pharmaceutical prices, developing countries would neither suffer nor benefit from patent policies. But the low statistical significance of the patent dummy variable can be explained by at least three factors. First, the authors do not distinguish between patent protection to pharmaceutical products and processes. For example, the authors listed South Korea and Zambia, as providing patent protection to pharmaceuticals when in fact they only provide such protection to processes. More importantly, the authors do not provide an idea of the extent of regulations; one could presume that the price control dummy variable picks up part of the impact of patents, i.e., dismantling price controls would result in a relatively higher price increase of patented drugs. Finally, one would expect patent protection to have

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[19] The ordinary least square estimation yielded the following results:

$$P = 38.53 + 1.43\ \underline{GDP}\ + 7.08\ PP - 15.72\ DPC - 11.12\ IPC + e$$
$$\quad\ (6.04)\ (6.69)\ N \quad (1.16) \quad (-2.30) \quad (-1.50)$$

$$R^2 = 0.78$$

where P = price index of pharmaceuticals; GDP = gross domestic product; N = population; PP = dummy for patent protection; DPC = dummy for price controls; and IPC = dummy for indirect price control measures.

particularly strong price effects in countries where the law clearly stands in favor of the patent holder. It is far from clear whether in developing countries patent rights are strongly protected by the law (see, for example, Gadbaw and Richards, 1988).

Probably, the most we can conclude from the figures in Table 4 is that in the industrial countries which enforced patent protection (United Kingdom, Netherlands, Belgium, France, Luxembourg, Denmark, Germany and the U.S.), also showed high prices of pharmaceutical products. In contrast, developing countries paid prices for pharmaceuticals which on average were only 42% of those paid in industrial countries providing patent protection. Furthermore, industrial countries like Italy and Japan that in 1975 did not provide patent protection for pharmaceuticals also showed quite a high price of pharmaceuticals. This observation lends support to the assertion that pharmaceutical companies charge what the market will bear.

Summing up, the previous section showed how increasing regulation had reduced effective patent life. In spite of this, investment in R&D by the industry has continued to increase, but productivity--measured in new drug approvals--continues stagnant. In this section we have argued that a number of institutional changes have facilitated competition from the generic drug industry and that generally such competition has a major downward effect on drug prices. Thus, the trend that emerges is one where profits of the R&D intensive pharmaceutical industry are squeezed by the double effect of government regulations and generic drug competition.[20] What strategies have the industry followed in order to confront this situation?

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[20] See Joglekar and Patterson (1986) for evidence of declining profits to R&D.

VI. Strategies of the R&D Intensive Pharmaceutical Industry

The R&D intensive pharmaceutical industry has followed a number of strategies in order to overcome the negative impact of the factors discussed in the previous section. These strategies can be classified as market-based or policy determined.

1. Market-based competition strategies

By market-based competition strategy, I understand a strategy that is developed and implemented within a stable framework of regulations and incentives. In this interpretation, the R&D intensive pharmaceutical industry has developed a number of strategies. First, several brand name companies have decided to produce generic drugs themselves. This has been done among others by Squibb, Warner-Lambert, American Cynamid and Ciba-Geigy. It has been estimated that these companies now supply 25% of the prescriptions for generic versions of drugs that have patents expire since 1980 (The Wall Street Journal, September 6, 1989, p. B1).

Another strategy has been to request the FDA to reclassify some of their patented drugs from prescription drugs to over-the-counter drugs. This would familiarize the customer with the medicine before patent expiration, thus reducing the extent of generic competition once the patent expires.

Other strategies have included mergers. Probably 1989 witnessed one of the most active merger years in the history of the pharmaceutical industry. The most visible mergers were those between Bristol Meyers and Squibb from the U.S., with combined annual sales of US$3.8 billion, and Smith Kline Beckman from the U.S. and Beecham, from the U.K. (now Smith Kline Beecham) with sales of US$3.6 billion. A common factor underlying this industrial restructuring appears

to be the increasing costs of R&D.[21] It would appear that many firms now consider that size is a most important factor to overcome the barriers imposed by high R&D costs and also benefit from economies of scale that apparently exist in the R&D process. These mergers would therefore increase the probability of coming up with new drugs with important market potential. While this is true, a declining number of pharmaceutical companies and increasing concentration might eventually affect competition--among other things--by reducing the number of competing drugs within therapeutic classes (Jadlow, et al., 1987).[22]

2. Policy-determined strategies

In addition to the market-based competition strategies that the pharmaceutical industry has developed, it has also organized itself to lobby and seek for higher rents thru policy changes. The industry has a powerful argument, namely, that the social rate of return of its investments in R&D is high. It is useful to quote Mansfield on his views of rates of return to innovation in U.S. industry generally "...practically all of the studies carried out to date indicate that the average social rate of return from industrial R&D tends to be very high. Moreover, the marginal social rate of return also seems high,

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21 This is often mentioned in the newspaper articles announcing the mergers. See for example, The Financial Times, August 4, 1989, article "In the Grip of Takeover Fever." Increasing drug competition within therapeutic categories has also been a factor. For example, it has been mentioned that sales of Smith Kline's anti-ulcer drug Tagamet was losing market to Glaxo's drug Zantac. In contrast, Beecham has two promising drugs: Eminase, for heart problems, and the anti-arthritis Deliflax (The Wall Street Journal, July 31, 1989), which as part of the merger agreement, Smith Kline is expecting to profit from.

22 As a consequence of these mergers, the proportion of total sales made by the four largest firms increased from 21.3% to 24.1%.

generally in the neighborhood of 30 to 50 percent. As in the case of studies cited in the previous section, there is a variety of very important problems and limitations inherent in each of these studies. But recognizing this fact, it nonetheless is remarkable that so many independent studies based on so many types of data result in so consistent a set of conclusions...." (Mansfield, 1989).

This conclusion implies that a marginal increase in R&D would be beneficial to society. In order to have the incentive to do this, the industry needs to appropriate a greater share of the rents produced by its innovations. This can be done in a number of ways but most importantly by seeking longer patent protection at home and stronger patent protection abroad. Section II reviewed the discussion of patent policies of developing countries; this section will review the subject in industrial countries. In addition, the industry seeks to obtain other preferential policies such as subsidies for R&D, additional funds for the FDA to accelerate the drug approval process, increasing the regulatory barriers to market generics by making the bioequivalency test between different brands come closer to one another, less stringent cost containment policies, less supervision on private sector pricing policies, lobbying against proposals for compulsory licensing, making it easier to transform prescription drugs to over the counter drugs, reduction in the burden of regulations for drug approval, etc.[23]

As the time required for approval of new drugs increased, and the patent office continued to arrive at a decision much faster than the FDA, the average effective patent life declined. For example, Eisman and Wardell (1981)

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[23] A presentation of these demands by the U.S. industry is made in Pharmaceutical Manufacturers Association (1987).

have estimated an average effective patent life for new pharmaceutical drugs of 13.6 years and 9.5 years in 1966 and 1979 respectively. This appears to be lower than in other countries. For example, for a common sample of drugs, in the U.S. it took from initial stage to FDA approval an average of 10.5 years, while it averaged only 5.4 years in other countries (Mossinghoff, 1987).

As the effective patent duration declines so does the private rate of return to R&D and the incentive to undertake this type of activities. In September 1984, after many years of lobbying by the industry, the Drug Price Competition and Patent Restoration Act was passed as U.S. law. It has two major components. First, it restores part of the patent life which drugs had lost as the pre-market testing process by firms and the FDA--as a consequence of the 1962 reforms-lengthened. It should be mentioned that this is the first time since 1861 chat the patent terms in the U.S. have been changed, and it changed in favor of one industry. The second major change of the Act is that it facilitates the entry of generic drugs.

The extension of patent life provided by the new law is equal to the sum of the drug application review time by the FDA plus one half the clinical testing time. The maximum extension is of five years and no extension beyond 14 years of effective patent life will be allowed. For the drugs introduced in the U.S. market between 1976 and 1981 the average effective patent life--had the law been applied during those years--would have increased from 8.9 to 11.8 years, i.e., by 33%.

This is a significant increase and had other things remained unchanged, the measure would have boosted the returns to R&D. But the other legislative change, facilitating the introduction of generic drugs into the market, has apparently compensated the R&D incentive effects of longer effective

patent duration. Under the new law, a generic drug company can market a product by demonstrating to the FDA that the drug is bioequivalent to the original one. This is a low cost experiment which contrasts with the lengthy and costly tests these generic companies were required to undertake. Because the tests undertaken by the original innovator were confidential, the FDA required similar tests by the generic drug company. But by demonstrating bioequivalency, these tests are not necessary; the new law has thus not only facilitated the introduction of generics but also eliminated duplicative testing.

What has been the impact of the 1984 Patent Restoration Act? In terms of the long-run incentives for R&D, the Act does not appear to have had a significant effect. Under different assumptions regarding the extent of the loss of sales to generic drugs, Grabowski and Vernon (1986) estimated that the returns to R&D of the innovative pharmaceutical firms, contingent upon the changes introduced by the new law remained on average quite unchanged; the faster generic drug approval process approximately counteracted the R&D incentives of longer effective patent duration. Nevertheless, in the short-run, the new regulations facilitating the approval of generic has implied that these drugs have taken a significant share of the market. In the aggregate, I mentioned that the combined U.S. market share of the 13 widely prescribed generic drugs has increased during the 1980s from around 30% to 60%. More specifically, generic drugs share in total prescriptions is now higher than 50% in the following therepeutic classes: cardiovascular, anti-diabetis, tranquilizers, anti-arthritis, antibiotics and analgesics (HKS, 1990). Summing up, a global analysis of the industry concludes that the short-run impact of the 1984 Patent Restoration Act has favored the generic drug companies (Kaitin, et. al., 1987).

Pharmaceutical firms of other countries have not remained passive to changes in U.S. regulations and patent protection. For example, for some time, the major EC pharmaceutical firms have been pressing the European Commission for longer patent protection. These firms claimed that longer effective patent protection in the U.S. and Japan, as well as longer gestation periods attributable to increasing regulations, makes the extension of effective patent protection necessary. The European Commission is now studying legislation that would extend such protection by two years and legislation providing this or higher protection is likely to be approved during 1990.

Finally, note that the further apart in time--from the moment research on a new drug starts--a dollar of income is earned, the lower the present value. Thus, for the same amount of time gained, a dollar of income from shortening the length of FDA regulations is worth more than a dollar of income gained from longer patent protection; remember that such a dollar is earned at the end of the patent life. Likewise, for any given drug, one dollar of earnings from the introduction of patent protection in developing countries is worth more than one dollar of earnings from the extension of patent protection in industrial countries.

Summing up, this section has shown that the R&D intensive industry has developed a set of complex strategies in order to meet competition from the generic drug industry. Part of this strategy is market oriented, but an important part is also policy determined. The industry is a highly regulated one, and each regulation is a source of negotiations between the industry and the government; over time this dynamic interaction between industry and government knits the web and nature of regulations. But among all of the regulations, patent protection stands high in the agenda of the industry;

patents sustain very high drug prices. In turn, these profits finance R&D whose output provide tomorrow's competitive edge. Section II showed the pressures the industrial countries put on developing countries for increasing patent protection to pharmaceutical drugs; this section shows that within industrial countries such protection has already been granted. Nevertheless, the time dimension of patents suggests that for similar levels of income, the introduction of patent protection in developing countries is worth more to brand name companies than the extension of patent protection in industrial countries.

VII. FINAL REMARKS

This paper offers a discussion to the question of why there are pressures on developing countries for introducing and/or reinforcing patent protection to pharmaceutical drugs. The story is that patent protection is an important component of a complex strategy developed by the R&D intensive pharmaceutical drug companies of industrial countries to meet market competition. For legal and economic reasons, patents--the paper shows--are fundamental instruments for allowing the drug-inventing companies to appropriate the returns from their innovations. Patents sustain high prices, which in turn provides rents to undertake further R&D, which in turn allows the invention of new drugs, etc., etc. In recent years, increasing drug regulations have implied that effective patent protection to the R&D intensive pharmaceutical drug companies has eroded. Furthermore, competition from the generic drug companies has increased quite significantly. Finally, the potential size of developing countries' markets for patented drugs is no loger trivial. Thus, restoring patent protection in industrial countries and making developing countries

introduce patent protection, has become part--albeit an important part--of R&D intensive pharmaceutical companies' strategies to regain market share.

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