5. The challenges of constructing pharmaceutical capabilities and promoting access to medicines in Mexico under TRIPS

Alenka Guzmán

According to Pavitt's taxonomy (1984), the pharmaceutical sector has been classified as an intensively scientific industry, where technology depends basically on the basic sciences of R&D. The pharmaceutical firms maintain their leadership by using intellectual property rights (IPR – patents, industrial secrets and trademarks). Patent systems in particular are of great importance to the pharmaceuticals industry, given the permanent risk of copying through the use of low-cost processes.

In this section, we explain the analytical framework of the pharmaceutical industry whereby the health system and the intellectual property system are seen jointly, through both a national (Bell and Pavitt, 1993; Lundvall, 1993; Nelson, 1993; Kim, 1997) and a sectoral innovation approach (Edquist, 1997; Breschi and Malerba, 1997; Malerba, 2002, 2004). Both the factors of demand[1] and supply[2] that contribute to innovations in the pharmaceutical sector refer to the elements that make up the national innovation systems and the sectoral innovation systems (NIS and SIS, respectively).[3]

[1] The demand side includes the size and evolution of the market (Schmookler, 1966), which are influenced by economic factors and socio-economic factors and affected by government policies, price capping, health expenditure budget and preventive health programs (Agrawal, 2000: 24).

[2] The determining factors influencing the supply are identified as the costs, alongside the productivity of the research and development (R&D) sector linked to the technological opportunities (Mowery and Rosemberg, 1989).

[3] The government, through macro-economic policies, promotes foreign financing, and through fiscal policies, regulatory and IP policies establishes the base for institutional incentives of R&D private investment and thus embarks on the path of innovation. Moreover, the human capital contributes to the technological development but also in this process it gains knowledge and additional abilities. Progress in the different scientific fields generates technological opportunities asso-

Technological backwardness in the developing countries is associated with the absence of technological capabilities, low levels of technological transfer and a low GDP per capita, along with few, or no, R&D efforts (Lall, 2003).[4] Under these circumstances, the strength of the patents becomes a barrier to the entry of imitative activity due to the high costs related to patenting. Therefore, the divergent patent systems are characterized by their low level of domestic innovative activity and are associated with a limited expenditure in R&D, poorly trained human resources, limited private industry participation, weak enterprise–institution links, and low-tech-laden exports. Furthermore, the diffusion ratio (penetration in USPTO) is characterized as being low (Aboites and Cimoli, 2002). Concerning the pharmaceutical sector, some emerging countries have reasonable industrial capabilities for high-level chemistry and produce their own raw materials. Other developing countries maintain a reasonable capability for the formulation of drugs and for productive activities; however, they must import practically all the necessary raw materials. But there are also countries typically characterized as being small and having no local production; in these countries, finished drugs are imported, leaving enterprises with marketing activities only. This last case reveals there are no productive capabilities whatsoever (Frenkel, 1978; Cepal-Naciones Unidas, 1987; Palmeira and Pan, 2003).[5]

Taking into account this analytical framework, we aim to find out how Mexico has managed the tools of intellectual property rights (IPR) in order to develop the pharmaceutical sector, by considering the special features of national and sectoral innovation and the health systems. Although the initial imitation capabilities of the local pharmaceutical industry in Mexico have been fostered by demand factors, especially in association with the growing importance of the public health sector, its

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ciated with a correct macro and intermediate environment, will promote the R&D activities along with innovation (Agrawal, 2000).

[4] Lall proposes a classification based on a technology intensive index derived from the national technological activity using two variables: R&D financed by productive enterprises and the number of patents taken from USPTO. Both deflated by the population and adjusted by economic size.

[5] In contrast, countries characterized by a high R&D expenditure in relation to local GDP, a well-developed education system that trains high-quality human resources and provides networks, thus creating favourable favorable synergies between enterprises and institutions, and whose exports have a high technological content, find favourable conditions for innovation activities within a strong intellectual-property framework (Lall, 2003); so they are in a convergent patent system (Aboites & Cimoli, 2002). Consequently, their pharmaceutical industries are capable of carrying out all the technological stages, going from basic research to the marketing of the drug (CEPAL, 1987; Frenkel, 1978; Palmeira and Pan, 2003).

development was characterized – during the import substitution industrialization (ISI) period (closed economy) – by the absence of several decisive supply factors. Indeed, there has been a lack of industrial regulation and IPR policies created with the objective of favouring R&D efforts to undertake steps on the path of innovation. The local pharmaceutical sector has not built up the necessary capabilities to integrate the industry by encompassing basic research, through the formulation and production of their own raw materials and drugs, to the marketing of the latter.

Within the export–industrialization pattern, the pharmaceutical sector is associated with a disarticulated national system of innovation in an unstable macro-economic and low-growth environment, with a prevailing lack of technological activities, insufficient human capital and marginal links between the universities and firms and cooperative networks. In this sense, we endorse the following hypothesis: the IPR reform seems to favour foreign --companies since the multinationals own solid innovation capabilities and profit from the opportunities to increase their partial production of drugs and their intra-firm trade, whilst appropriating the R&D efforts carried out in their home countries. However, for local firms, the strengthening of patents could, in fact, deepen their technological dependence and impede higher development steps, unless this country undertakes an important effort to build national and sectoral systems of innovation, and most importantly, productive, export-oriented specializations.

The chapter is organized into four sections. Firstly, we proposed an analytical approach regarding national and sectoral innovation and health systems vis-à-vis the intellectual property system. Secondly (the next section), we characterize the Mexican pharmaceutical industry in the context of its intellectual property system and its health system. Thirdly, we identify the technological and innovative capabilities in the pharmaceutical industry in Mexico. Finally, we evaluate the impact on pharmaceutical innovation and performance along with access to drugs in Mexico, by considering the IPR system and analyzing the innovation framework of the pharma-health systems.

MEXICO'S PHARMACEUTICAL INDUSTRY, INTELLECTUAL PROPERTY SYSTEM AND HEALTH SYSTEM

Development Background

From the 1950s to the 1980s, industrial organization in Mexico's pharmaceutical sector was characterized by: i) the presence of a

reasonable level of national capital in both the pharmaceutical and pharma-chemical sectors; ii) the absence of patents in the pharmaceutical area; iii) elevated tariffs on the importation of raw materials for the pharma-chemical sector; iv) priority of marketing approval to the medicines of local producers; and v) a significant increase in the number of medium sized and family structured national companies. This type of pharmaceutical and pharma-chemical model, which is orientated to the production of generic medicines and, in some cases, to the exportation of active ingredients of expired patents, is denominated as "later-follower" (Katz, 1997).

In the Mexican pharmaceutical industry, real imitation capabilities were developed to produce new pharmaceutical products, which allowed the country to cover its basic domestic demand for medicines (CEPAL, 1987).[6] Nevertheless, the Mexican industry never developed medicine exportation capacities, nor did the multinationals show any interest in exporting their products to other countries from their Mexican bases (Brodovsky, 1997). The knowledge and the abilities of the pharmaceutical companies came basically from two sources: licenses and (free) technology in the public domain, given the absence of a patent system in the pharmaceutical sector. In collaboration with public universities, important chemical synthesis laboratories developed basic research and, in some cases, achieved new molecules.[7]

Despite the Mexican inventive activity in the drugs and medical technological category, it remained highly incipient and marginal with respect to the industrialized nations, and patents formed no part of the development strategy. The USPTO granted, between 1963 and 1979, just 63 patents to Mexican holders in the drugs and medical category,[8] revealing the embryonic nature of the advance in the development of capabilities in the scientific and technological sectors of the country.

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[6] Medicinal imports were less than 2 percent of the whole national market consumption (Bradovsky, 1997).

[7] The most relevant endogenous innovation, on an international scale, was the case of Syntex with the production of steroids (Gereffi, 1986). However, the strong technological dependence on foreign firms was constant in the local manufacturing plants in the pharma-chemical and pharmaceutical sectors.

[8] The 63 patents granted by USPTO to Mexican holders in Drugs and Medical category between 1963 and 1979 reached 6.6 per cent of the all-sector total patents granted (956); this number has grown to 50 patents in 1980–1990 and to 71 from 1991 to 2002 (the period of adoption of TRIPS in Mexico). According to Jaffe and Trajtenberg (2002), the classification Drugs and Medical includes Drugs, Surgery and Medical Instruments, Biotechnology and Miscellaneous Drugs and Medical.

In Mexico, efforts to develop an integrated productive chain encompassing R&D related to the development of new molecules and the commercialization of new drugs were impeded by the technological intensity of the international sector and local firms' general incapacity to incorporate technological progress (Brodovsky, 1997). Moreover, the government failed to design adequate policies for the generation of a favourable macro-economic and institutional environment in which the development of scientific and technological capabilities would lead to innovation. This fragility was ever more apparent with the opening up of the economy, the dismantling of the protectionist structure and the strengthening of the patent system. In this new institutional environment, with the enormous technological and innovative gap in both scale and financial capacity, the local companies were pitted against the large, multinational pharmaceutical firms and thus registered ever increasing losses due to the increased competition combined with technological dependency.

The Importance and Industrial Organization of the Pharmaceutical Industry in Mexico

Currently, Mexico has almost a quarter of the resident population of Latin America and contributes 29 percent of the total regional GDP (CEPAL, 2008). The country's pharmaceutical market is classified among the "top ten" world markets and top in Latin America, with a value of 13.5 billion US dollars in 2006 (MOITI, 2006); its sales represent 37 percent of Latin America's total sales (Chávez, 2007). From 1994 to 2006, the pharmaceutical market registered an annual growth rate of above 10 percent (National Pharmaceutical Industry Chamber, CANIFARMA – Cámara de la Industria Farmacéutica). The dynamic growth of Mexico's medicines market is associated with, among other factors: i) an environment with a strong patent system for pharmaceutical processes and products since 1991; ii) commercial agreements signed with 33 countries, one of the most important being the North American Free Trade Agreement (NAFTA); iii) low production costs – 50 percent lower than in other countries; iv) the high professional qualifications of the personnel; v) related to the preceding factors, the strong growth in foreign direct investment (FDI) ;and vi) being the regional leader in the export of pharmaceutical products to European countries and the United States (calculated to be 1.5 billion US dollars in 2007).

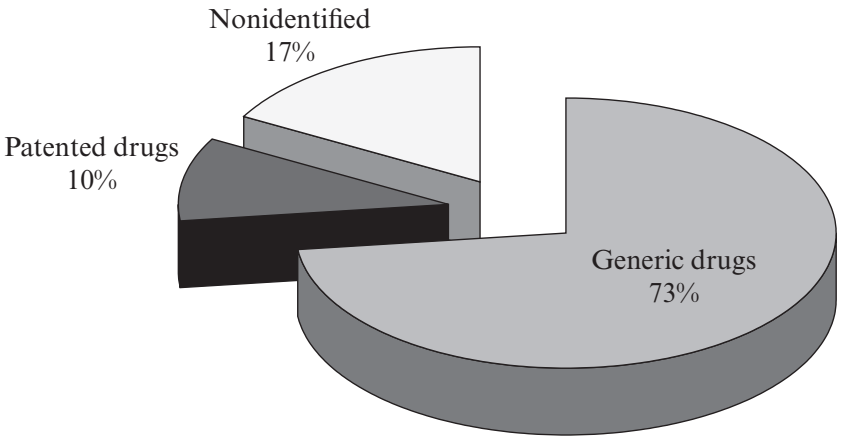
The Mexican pharmaceutical industry represents 1 percent of the country's total GDP and 2.7 percent of manufacturing GDP. According to CANIFARMA, the industry is made up of 224 pharmaceutical labo-

ratories owned by 200 companies, 46 of which are multinationals.[9] These companies generate nearly 50,000 direct jobs and an additional 47,000 indirect employment opportunities. Nearly three-fifths of the direct job total (57 per cent) are positions related to sales and administration, 37 percent are in production and R&D activities, whilst the remaining 6 percent are in other related activities (Mexican Pharmaceutical Industry Association – AMIF).

The pharmaceutical industry has a high market concentration, in which foreign companies account for 68 percent of the total market; local companies make up the remaining 32 percent. Of the 'top ten' companies in Mexico's pharmaceutical market, 9 are foreign multinationals (MNS), the most important being Pfizer, Bayer and Merck Sharp & Dohme, with sales of over 500 million US dollars in 2003; the only Mexican company in the 'top ten' is Laboratorio Senosian, which registered sales of 131 million US dollars over the same period; of the nine foreign MNS, five are US based (Wyeth, Eli Lilly and the top three mentioned above), two are German (Boehringer Ingelheim Prometo and Merck), one is Swiss (Novartis) and the other is French (Sanofi-Synthélabo, now Sanofi-Aventis) (CANIFARMA; *El Asesor*, cited by WPM, 2005). The top 35 players in the Mexican market account for 80 percent of the total sales; among them there are six national participants, the rest being multinational pharmaceutical firms (Scripps Pharmaceutical Industry League Tables, 2004).

The market segmentation in relation to the private and public sectors is 80 per cent and 20 per cent, respectively. With regard to the public sector, Mexico's Ministry of Health has a total of 800 marketing approval medicines, of which 70 percent are national products distributed by ANAFAM. Four fifths of the medicines acquired by the public health sector are generic products, the principal generic producers being national companies. Meanwhile, ANAFAM states that 80 percent are purchased from 50 national suppliers, whose sales to the government represented approximately 545,500 US dollars in 2006. Of the medicines included in the country's public-sector basic national basket, 776 are generic medicines, purchased on the basis of efficiency, quality, security and accessibility. The strong competition for this market can be seen in the fact that for each contract awarded there are 20 companies taking part in the bidding process and, in just 10 percent of this public market, 20 of the most

[9] Other sources say that there were 390 domestic and transnational companies manufacturing pharmaceutical products (Massachusetts Office of International Trade & Investment – MOITI, 2006, www.mass.gov/moiti).



Source: Martínez 2010.

Figure 5.1 Shares of generics and patented medicines in the Mexican public market by units, 2009.

important companies are represented (OECD, 2005: 66). The government allocates 56 percent of its drug procurement budget to medicines patented by the MNS, 29 percent to generics and 15 percent are not identified (Martínez, 2010). In terms of units, however, these financial resources buy 10 percent patented drugs, 73 percent generics and 17 percent are not identified (see Figure 5.1).

Public institutions like IMSS and ISSSTE allocate nearly one third of their drugs expenditure to generics, representing three quarters of total units bought. In contrast, they spend more than a half their budget on patented drugs, representing only 10 percent of units on average. The case of Petróleos de México (PEMEX) is a little different because this institution spends more on generics and less on patented medicines. The public institutions belonging to the Social Security system (SS) spend mostly on patented medicines (89 percent), obtaining 63 percent in units, and less on generics (6 percent), obtaining 36 percent in units; this could be because those institutions have high therapeutic specialization and use new drugs to treat diseases and surgery interventions with efficacy. See Table 5.1.

Prescription drugs represent the largest share of the country's private medicine market, with 84.2 percent of total sales; meanwhile, over-the-counter products (OTC) account for the remaining 15.8 percent of total sales (World Pharmaceutical Markets, 2005). Associated with the importance of prescription medicine sales, patented medicines make up

Table 5.1 Shares of generics and patented drugs in the Mexican public market, 2009 (per cent)

	Units			Value		
	Generic drugs	Patented drugs	Non-identified	Generic drugs	Patented drugs	Non-identified
Public market	73	10	17	29	56	15
IMSS	74	8	18	32	50	18
ISSSTE	73	12	15	27	60	13
SS	36	63	1	6	89	5
PEMEX	70	23	7	49	44	7

Source: Martínez 2010.

87 percent of the total sales.[10] Its part, the generics market (denominated interchangeable generics) has relatively low market participation (2.7 per cent), while the non-bioequivalent drugs (known as 'similar' generics) market share reached one tenth of total sales in 2002.[11]

The market for 'similar' generics in Mexico was terminated in 2010, as new health regulations entered into force concerning the renewal of drug approvals procedures applicable to all pharmaceutical products every five-year period by the Federal Commission for the Protection against Health Risks (COFEPRIS – Comisión Federal para la Protección contra Riesgos Sanitarios), according to article 376 of the General Health Law. For the approval of medicines, the stringent regulations of COFEPRIS require: i) the official standards for good practice in the manufacture of medicines, NOM-164-SSA-1-1998; also, primary materials, especially active ingredients of the drugs, must follow the norms; ii) the bioequivalence and bioavailability tests, assuring the necessary concentration, stability, security and quality of production process and products;[12] iii) clinical trials which must verify the therapeutic efficacy; iv) conditions of quality,

[10] The above probably explains the elevated prices of the medicines, much higher than those of the generics; nevertheless, the orientation of the health systems favoured the prescription of generically formulated medicines.

[11] The interchangeable generic medicines are those that have proved their bioavailability and their bioequivalence, thus making them exactly the same as the originals. The 'similar' products are generics that have not necessarily undergone the aforementioned studies.

[12] The bioequivalence and bioavailability tests are going to be carried out by 'third party' laboratories under the authorization of the Ministry of Health.

efficacy and security must be maintained during the period of marketing of the product; and v) that COFEPRIS verify that the Mexican Intellectual Property Office (IMPI) has not, in the IMPI Gazette, published a patent on the chemical entity of the drug in question.[13]

In September 2005, COFEPRIS counted nearly 40,000 pharmaceutical products registered, of which 7,000 were on the market and only 3,100 were interchangeable generics. As a result of recent reforms, as of the end of 2010 there will no longer be any non-bioequivalent drugs on the market but only interchangeable generic products that meet the high requirements of the developed countries' pharmaceutical industry, and patented medicines.

Another important change in the pharmaceutical industry and health regulations is the cancellation of the 'plant request' as a condition for the introduction of medicines into the Mexican market (9 August 2009).[14] COFEPRIS took this measure when the country was seen as one where HIV antiretroviral prices were among the highest in the world, during the World HIV/AIDS Conference in Mexico in 2008. According to the Mexican government, the goal of this measure is to facilitate the introduction of cheaper medicines, even through importation, and improve the sector's competitiveness. Therefore, for the assurance of the best production practices, quality and safety of drugs, COFEPRIS sends health supervisors to visit the foreign plants where the medicines imported into Mexico a produced. As a result of the cancellation of the 'plant request', there have been some applications by pharmaceutical multinationals, which did not have production plants in Mexico, to market drugs in therapeutic categories for cancer and metabolic diseases. Although this new regulation favors access to cheaper medicines, it also contributes to deindustrializing this sector, reducing some MNS technological knowledge spillovers and reducing employment.

Foreign Direct Investment, Trade and Market Specialization

Mexico experienced a significant increase in foreign investment in the 1990s. Between 1999 and 2006, foreign direct investment (FDI) increased over 200

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[13] The adoption of the COFEPRIS–IMPI linkage on the renewal of the drug approval every five years has provoked a big debate among the local firms because it gives the possibility of delaying the entrance of generics in the domestic market. We analyze this issue later.

[14] The plant request was a policy measure to incentivize pharmaceutical MNS to invest in Mexico. Through this requirement any company must have a production plant in Mexico to market their products.

percent, reaching US$346 million (Chávez, 2007). This investment came mainly from five of the most industrialized countries (the United States, 31 percent; the Netherlands, 10 percent; Germany, 9 percent; Switzerland, 8 percent and Spain, 6 percent) and was destined mainly for the capital, Mexico City, the State of Jalisco and the State of Mexico.

Mexico soon became a major player in the export of medicines not only to Central American and Caribbean nations, but also to industrialized countries such as the US and Germany. However, the importation of raw materials, along with final products, increased substantially. The latter represents 13 percent of total sales, of which a quarter came from the Unites States (World Pharmaceutical Markets, 2005 and 2006).

The specification of the type of imports has great relevance in the sense that it permits identification of the areas in which countries are self-sufficient or not, and thus the areas where they possess lesser productive and competitive capacities. Although the importation of retail medicines is relatively high (in 2004, 36 percent of total imports) the majority of the imports were concentrated in the medicine sector for OTC sales (60 percent), whilst the importation of semi-finished products was relatively marginal (4 percent). The importation of retail medicines was carried out by both local and foreign-based companies. With regard to final products, the majority of imports were purchased from affiliated multinational pharmaceutical laboratories, which indicates that several of these companies produce only certain products within the country and import the remainder.

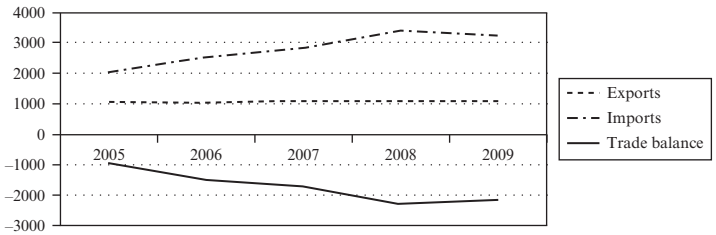
In Mexico, the majority of the imported products arrive from the US or the European Union countries, which represent 86 percent of the total imports; a predominance of North American partners is evident. The remaining 14 percent of Mexico's imports come from China, India, Argentina and other countries.

Despite the important growth registered in Mexico's pharmaceutical markets in recent years, fragilities can be seen once the balance of trade is analyzed. Thus, although exports have registered substantial increases, imports have grown even more. As a consequence, the commercial balance with regard to pharmaceutical products, from 2000 to 2002, shows a deficit. In relation to the type of products, the deficit is greater regarding raw materials (55.8 percent). This implies that the greater part of the molecules, and active ingredients, necessary for the fabrication of medicines have registered net imports. This is associated with the closure of pharma-chemical plants. In Mexico, the net imports of active ingredients contributed with 55.8 percent of the total negative balance. In 2002, Mexico registered high negative commercial balances in raw materials related to vaccines, other antibiotics and tetracycline. The deficit in the semi-finished products represented 8 percent of the total negative commercial balance. The deficit

Table 5.2 Mexican trade balance in pharmaceutical sector, 2005

	Trade deficit (thousands of US$)	Per cent
Raw materials	–421,265	55.8
Semi-finished medicaments	–60,712	8.1
Retail medicaments	–272,711	36.1
Total	–754,688	100.0

Source: World Pharmaceutical Markets, 2005.



Source: Institute of Pharmaceutical Research & Innovation, A.C. with INEGI and Banxico databases.

Figure 5.2 Evolution of exports, imports and trade balance in Mexican medicines market, 2005–2009 (millions of US$).

regarding the antibiotics is of particular relevance. The negative balance of retail medicine sales is also substantial (36.1 percent); Mexico has a deficient production in hormones, other antibiotics and vitamins. See Table 5.2.

According to other sources, the negative trade balance in medicines was higher in 2005 (981.5 million dollars); moreover, it increased at an average annual rate of 21.97 percent from 2005 to 2009 because imports have risen faster than exports (see Figure 5.2). This loss tendency in the trade balance highlights the growing technological external dependency of the Mexican pharmaceutical sector. While in 2005 national production covered 90.0 percent of the apparent national consumption of medicines in Mexico, in 2009 it fell to 80.3 per cent.

Intellectual Property System

After several decades of a lax intellectual property rights (IPR) system, particularly in the pharmaceutical industry (products and processes),

Mexico carried out IPR reforms in 1991, just prior to the signing of the NAFTA, in 1992, which entered into force in January 1994 (Guzmán and Zúñiga, 2004). Although the entrepreneurs in the national pharmaceutical sector were instructed by the government in 1987 (the year in which Mexico joined the GATT) to develop their own generic production capacities within a period of ten years, along with the strengthening of the intellectual property rights, the principal players were taken by surprise by the premature adoption of the TRIPS-compliant Law on the Promotion and Protection of Industrial Property (LFPPI – Ley de Fomento y Protección de la Propiedad Industrial) (Guzmán, 2005). The Mexican government, under pressure from the American pharmaceutical companies, enforced IPR in this industrial sector, including the 20 years validity period. This new IPR environment would guarantee the flow of investment and commercialization within Mexico, even if the new products of pharmaceutical firms were always introduced into the Mexican pharmaceutical market, but now without the risk of imitation. And, as if this was not enough, the reform also included the 'pipeline' system, which allowed for a retroactive period for product registration, even in cases where the knowledge was in the public domain, a fact that several companies exploited (De la Mora, 2005).[15] 'This was a requirement of NAFTA, which goes further than the limited marketing rights provided during the transition periods by TRIPS' (Maskus, 1997, cited by Moïse and Docteur, 2007: 10).

Also, this IPR reform included acceptance of a second therapeutic use of the molecules, which meant the implicit acceptance of the extension of the life period of the pharmaceutical patents. Suddenly, patent extensions are being demanded in developing countries as a compensation for the delays during the process of application and granting, but also for the length of time required for conducting clinical trials in order to obtain marketing authorization (Moïse and Docteur, 2007: 11). Faced with these new circumstances, and in the absence of an active industrial policy for the pharmaceutical sector, only a few companies entered into research and development (R&D) activities, in these cases strengthening the development of expired patents, or those in the public domain, or actually developing certain niche markets with regard to innovation.

By using compulsory licenses, Mexico could manufacture generic copies of patent medicines (Articles 70 and 77 of LFPPI). The compulsory license can be granted if the patented drugs have not been produced in Mexico

[15] According to article 12 of LFPPI, the applications for pipeline patents could be applicable to any pharmaceutical patent prior to 1991 in any country which has signed the Patent Cooperation Treaty.

within four years of the priority date or three years after the patent was granted. The compulsory license can be denied when the patent holder or a company licensed to import the drug has imported the product. With those requirements, under article 70 it becomes extremely difficult to obtain a compulsory license. In the case of a national emergency related to a health crisis or shortage of medicines, a compulsory license can be granted to another laboratory in accordance with Article 77 of LFPPI. Nevertheless, despite important cases of national health crisis in Mexico (especially the serious extent of the influenza AH1N1 since April 2009 in Mexico),[16] or the significant growth of public health expenditure on antiretroviral drugs to treat HIV/AIDS or other medicines for cancer and diabetes, among others, there has not been one compulsory license issued in Mexico over the last 14 years (Moïse and Docteur, 2007).

However, the adoption of a strong patent system was not enough for US companies to ensure that their Mexican counterparts would not infringe their patents. Through the Pharmaceutical Research and Medical Manufacturers of America (PhRMA), in 2003 they requested that the Ministry of Health and Assistance – Secretaría de Salubridad y Asistencia (SSA) – make drugs marketing approval conditional on the linkage of patents. Therefore the Regulation of Health Inputs of COFEPRIS amended article 167, adding 167 bis and also article 47 of the Patent Law of IMPI, adding 47 bis, both published in the Federation Official Gazette on September 19, 2003. According to article 167 bis, the linkage means that COFEPRIS will deny the generic medicine approval or license to market the drug in the event that a chemical entity patent exists. The request of linkage was finally incorporated into the reforms of marketing approval procedures in 2005 when the IMPI published the agreement of the rules to make up the list of the drugs to be published six-monthly in the IMPI Medicines Gazette regarding article 47 bis.[17] We must emphasize that article 6 of this agreement stipulates that the list will not include drug

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[16] The case of AH1N1 influenza in Mexico 2009 had important health repercussions not only in this country but also in other countries. Even though it was a new influenza strain and the vaccine wasn't yet developed, the medicine adequate for the immediate treatment of this influenza was the active ingredient ozeltamivir, known commercially as TamifluÒ and produced by Roche, the holder of the patent. The government could promote the production of the ozeltamivir generic version in the public or private laboratories through a compulsory license.

[17] This IMPI Medicines Gazette was a *Publication of Drugs Patents in force according to 47 bis of Regulation of the Industrial Property Law*, not the ordinary IMPI Gazette which publishes all the patents monthly. In order to elaborate the list of allopathic drug patents in force at the IMPI will consider the opinion of the CANIFARMA (Federation Official Gazette, February 4, 2005).

patents protecting product or formulation processes. The use of information from the drugs patents list will be used exclusively for COFEPRIS and IMPI linkage purposes (article 7).[18]

Although Mexican firms could not take advantage of the transition period for TRIPS compliance (as India and China did), because of the unexpected early IPR reforms of 1991, they agreed to respect the new IPR and more precisely the new Patent Law. But the reform of Patent Law in 2003, associated with the generic drugs approval, was seen by them as too stringent (even compared to those adopted in developed countries) and also as an entrance barrier to domestic generics. Indeed, since the 1990s, international innovation in molecules has decreased. The big pharmaceutical firms have followed a strategy of development by looking for new formulations, new uses, new dosages, new packaging or new chemical presentations in existing chemical entities. Nevertheless, even if there is an improvement in medicines and/or new findings in therapeutic uses, it does not signify the introduction of new molecules or chemical entities; the pharmaceutical companies extend the life of an existing patent or apply for a new patent. Consequently, the monopolistic price will be extended and the possibility of the general public and even the government accessing cheaper generic medicines, under a competitive environment, will be postponed even longer.

Additionally, drug approval applications meet with slowness and inefficiency. Many of them are not approved by COFEPRIS, owing to the lack of technological or IPR knowledge resulting from the absence of experts. Moreover, the lack of agreements between the ANAFAM (domestic firms) and AMIIF (MNS) associations, both belonging to CANIFARMA,[19] to establish jointly with the IMPI the list of patents protecting molecules, does not favor the right decisions. In this context, some MNS pharmaceutical firms have claimed in the courts or the Supreme Court of Justice the inclusion of patents which do not protect chemical entities and are excluded from the list of IMPI Medicines Gazette. Court decisions are frequently made with absolute ignorance in relation to the subject. The lack of judges skilled in IPR matters impedes the right decisions being made; either the

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[18] Moïse and Docteur (2007: 11) point out that "The purpose of the Gazette is to reduce IMPI's burden in resolving pipelines cases by providing a link between the patents information on drugs that IMPI holds and the request for marketing authorization received by Ministry of Health."

[19] ANAFAM is the National Association of Drugs Manufacturers (Asociación Nacional de Fabricantes de Medicamentos); AMIIF is the Mexican Association of the Research-Based Pharmaceutical Industry (Asociación Mexicana de Industrias de Investigación Farmacéutica). Finally, CANIFARMA is the Chamber of the National Pharmaceutical Industry.

court calls for legal protection because the judges are convinced that the patent concerns a chemical entity[20] or suspends the unpublished patent in the Gazette on the grounds that it has been extended in other countries even though not in Mexico.[21] Sometimes during the litigation process the IMPI decides to include the patent in question in the Medicines Gazette, impeding the marketing approval. In other cases, COFEPRIS refuses or suspends the drug approval because of a lawsuit and this gives a practical extension to the patent concerned. Therefore, according to some local firms, almost one third of the drugs published in the Medicines Gazette do not belong to new chemical entities.

Health System

In 2007, life expectancy in Mexico rose to 76 years (73 years for men and 78 for women) (World Health Statistics – WHO, 2009).[22] The total expenditure on the health sector represented 6.6 percent of the country's GDP in 2005, which is one of the lowest levels of all the signature countries of the OECD (WHO, 2009). The government continues to make an important contribution to total health expenditure, although this is decreasing; its share dropped from 46.6 per cent in 2000 to 45.2 per cent in 2008. Still, health expenditure related to the activities of the Social Security system is substantial. Public health expenditure in 2006 reached 44.2 percent of total health expenditure and it was made up of 31.8 percent from the federal government, 6.2 percent from the states' governments and 62 percent from the Social Security institutes. Meanwhile, private sector health has increased its share in total health expenditure, rising from 53.4 to 55.8 percent between 2000 and 2006. Total health expenditure per capita, on average, was 527 US dollars in 2006 and 420 US dollars in 2008. In terms of dollar/peso purchasing power parity, total health expenditure per capita in the same year was 778 dollars; 55.8 per cent was private and 44.2 per cent public (WHO, 2009).[23]

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[20] This is the case with Terbinafina (Patent 182129) and Omeprazol (Patent 194930) among others.

[21] This is the case with Clopidogrel (Patent 178820) and Micofenolato de mofetilo (Patent 177872).

[22] According to OECD, life expectancy in Mexico increased from 63 years in 1970 to 70 years in 1980; and from over 74 years in 1990 to over 76 years in 2000 (OECD, Health Data 2004). Regarding child mortality rates, they stand at 20.5 percent and in the case of maternal mortality rates the figure is 65.2 percent, indicators superior to those of the average in the OECD countries.

[23] The greatest differential in the calculation considered by the PPA may be related to the appreciation related to the peso / dollar exchange rate in the aforementioned years.

Nevertheless, although the Social Security system, and in particular the Ministry of Health, seem to have influenced decisively, among other factors, the increase in life expectancy, there is a significant level of backwardness in the coverage and financing of health, apparent in several indicators.

The creation of the national health system dates back to the post-revolutionary period and was linked to the need to have government intervention in social policies. Particularly, in the health sector the main objective was to improve hygiene in urban zones and to combat contagious diseases. In this context, the SSA was created. From the 1940s, the principal institutions that make up the present health-service sector were created.[24] Through this system, with social welfare adopted as the main focus, access to health services for an ever greater number of the country's poor was proposed, as well as the establishment of general public health policies and the administration of the Social Security system (SS) (including health services) for unionized workers or labor groups (IMSS). The SS was financed under a tripartite regime (government, employers, workers) and the allocation of resources and access to health services was based on the political and economical influences of distinct union groups (union cupolas) and were essentially based in urban zones. In contrast, the SSA was financed solely by the government and supplies health coverage to all those who had no right to services from the SS. The inequalities regarding the financing and the allocation of resources between the two systems was apparent in the differences in the services supplied, as was the significant lack of coverage in the rural zones of the country. As a result, from the 1960s, Mexico's health policies have been undertaken through several programs with different denominations: IMSS–COPLAMAR, IMSS–Solidaridad and currently IMSS–Oportunidades, aiming to reduce the unbalanced access to health services. Thus, the obligatory coverage of temporary and rural workers was extended, and there was also an increase in the partial access to loans from the Social Security Institute to groups based in rural areas and to players in the informal economy. Since the 1980s, there has been a concerted effort to decentralize the services supplied by the SSA towards the country's states, but this idea was severely affected by the economic problems suffered throughout that decade.

Once again, in the 1990s, efforts were made to continue the decentralization process involving the transfer of functions, responsibilities and

[24] In the 1940s, the Ministry of Health and Assistance (SSA) and the Mexican Social Security Institute (IMSS) were founded. In 1960, the Institute of Social Security Services of the State Workers (ISSSTE) was created.

financial resources to the states, especially in the context of the 1994–1995 financial crisis, during which the proportion of the Mexican population under the poverty line increased substantially, reaching 52 percent, and as a consequence the lack of medical coverage was much more evident. A further point is the incidence of nutritional problems in children below the age of 12 and in pregnant women, which severely affect both the physical development and emotional state of the victims.

The Reform Plan for Health Services 1995–2000 established, among other objectives, an increase in the coverage of health services supplied to the non-insured sector of the population through programs including the Program for Increased Coverage (PAC). The National Health Program 2001–2005 went further with the health coverage policies (OECD, 2005).

The Popular Health Insurance (SPS – Seguro Popular de Salud) was created as a pilot health program in 2001 to provide coverage for workers in the informal sector under the National Health Program 2001–2005. In 2004 the SPS became part of the system of Social Health Protection with the goal of being the main vehicle for assuring the entire social security coverage. The SPS proposes proportional, progressive coverage for a package of interventions and certain very costly treatments. The financial resources for this program are supplied by state and federal governments, alongside complementary payments by the families involved – on an income-based scale. With this voluntary health insurance scheme, the aim is to reduce the inequalities in the social security coverage throughout the country's states (OECD, 2005).[25]

SPS acquired relevance if we consider that 15 million people are self-employed, i.e. one quarter of the working age population (OECD, 2005), around 20 million individuals are working in the informal sector (Ceballos, 2003) and 40 million people were uninsured in 2002. Nowadays the SPS relies on four main health programs, following the goals of the Millennium: 1) the Health Assurance for the New Generation, which concentrates on diseases and disabilities in children under 5 years old; 2) Healthy Pregnancy Strategy to assure the adequate care of pregnant women; 3) Catastrophic Expenditure Protection Funds assigned to cover the high speciality services; and 4) 'Oportunidades' Program to give coverage to families in 266 medical interventions (including hepatitis, oste-

[25] The financial sources of SPS are: i) social fee, 3.92 per cent of minimum wage of Mexico City – mwMC; ii) federal solidarity fee, 1.5 times the social fee (5.88 per cent of mwMC) and iii) state solidarity fee, 0.5 times the social fee (1.96 of mwMC). The federal and state governments' financial contributions are assigned: 89 percent to the affiliates by state; 8 percent to the catastrophic expenditures fund and 3 percent to the budgetary provision fund (Chertorivski, 2010).

Table 5.3 Numbers of people affiliated to Popular Health Insurance, 2004–2009

Year	People (millions)	Children (millions)*	Women**	Families (millions)***
2004	5.3			
2005	11.4			
2006	15.7			2
2007	21.8	0.82		2.5
2008	27.2	1.90	188	2.9
2009	31.1	3.00	568.3	3.2
2010 Feb	32.7	3.10	717.2	5

Notes:
* Children affiliated to the Health Assurance Program for the New Generation
** Women affiliated to the Healthy Pregnancy Strategy
*** Families affiliated to SPS receiving coverage of the Program 'Opportunities'

Source: Chertorivski 2010.

oporosis and arthritis). Although the number of people affiliated to SPS has increased, between 2004 and 2009 there has been a high turnover in the people affiliated, according to health needs. See Table 5.3.

Although the Popular Heath Insurance program was created to reduce backwardness in coverage with regard to health services and access to medicines, this program has some severe limitations. Firstly, this is due to the requirement for large quantities of additional financial resources in an environment of reduced economic growth, an absence of major fiscal reform that guarantees government income (not from the petroleum sector) and greater financial pressures from the country's pension scheme. Concerning the acquisition of low cost drugs, the SPS buys the generics by bidding at the lowest prices, but in the case of patented medicines they accept the monopolistic price. Secondly, the SPS only provides coverage for basic services and so has only limited control as regards potentially catastrophic risks. Recently, the SPS has included the treatment of HIV, diabetes, cervical and breast cancer, child and adolescent cancer, cataracts, bone-marrow transplants and intensive care for new-borns; in all these costly and serious areas, the SPS provided services to 60,561 persons in 2006 and 114,773 in 2009, spending 330.5 million dollars in the latter year. Thirdly, given the fact that the services of the program are provided in the same institutional premises as the Social Security, there is potential for differentiation in the quality of the services provided to those of the population with insurance coverage and those without SPS (OECD, 2005).

Epidemiology

In addition to the characteristic complaints resulting from under-development and poverty, in Mexico, there are also illnesses associated with industrialized countries and that are common in the elderly population. The significance of these different illnesses is reflected in the size of the market within the therapeutic category in terms of sales of drugs. So, as can be seen in the magnitude of sales, expenditure is higher for medicines that correspond to the treatment of food/metabolism problems (which include illnesses found typically in poor countries – for example malnutrition, including obesity problems;[26] and rich countries – for example diabetes,[27] bulimia), central nervous system and cardiovascular diseases. Smaller but no less important are the market segments that correspond to the categories of respiratory therapy and infectious diseases, which belong to the category of medicines used in the treatment of the everyday illnesses of a poor population (intestinal infections, malaria, tuberculosis, etc.).

Of the 31 OECD countries in 2006–2007, Mexico had the highest mortality rates, behind the eastern European countries (Estonia, Hungary, the Slovak Republic and Poland), the rates being estimated at between 138 and 178 per 100,000 inhabitants (see Gay et al., 2011, who quote OECD estimates). Illnesses related to the circulatory system have been identified as the principal cause of death in Mexico; in the year 2006, of the total number of deaths, 43.9 percent were associated with these types of illnesses. Other illnesses associated with a large number of deaths were: cancers (14.2 percent), infections diseases (12.4 percent) and endocrine, nutritional and metabolic system diseases (5.9 percent). However, an alternative methodology has found endocrine, nutritional and metabolic system diseases to be the first cause of death (26 percent) (see Gay et al., 2011). The increase in the number of AIDS patients is of great concern owing to the high cost of care for this type of patient, given the fact that the latest generation of drug treatments have a greater effect and are patented. Among the illnesses related to poverty, in order of importance, are: influenza, diarrhea in both the under-5 age group and the over-5 age group, along with pneumonia. To conclude, Mexico is a country in which illnesses associated with under-developed countries are prevalent, but

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[26] According to WHO (2010), Mexico ranks second globally in child obesity. This condition could increase several kind of illness in the Mexican population, such as cardiovascular diseases and diabetes, and subsequently create financial burdens for government heath spending.

[27] Mexico had 4 million people with diabetes in 1995, and 12 million people are expected to have diabetes by 2025 (IMS, 2010).

illnesses associated with the industrialized nations are also an important part of the equation.

TECHNOLOGICAL AND INNOVATION CAPABILITIES IN THE PHARMACEUTICAL INDUSTRY

In this section, we identify the technological and innovative capabilities of the pharmaceutical industry in Mexico. Our research is based on two innovation surveys carried out by the INEGI-CONACYT during the year 2000 and the years 2004–2005, with regard to applications and patents granted in the USPTO and those granted to residents and non-residents approved by the National Patents Bank (BANAPA) of the Mexican Institute of Intellectual Property (IMPI), alongside interviews held with qualified industry participants.

One of the first aspects of concern is: Who innovates and how much is devoted to innovation within the pharmaceutical industry? In Mexico, in the year 2000, only 39 percent of the interviewed establishments reported undertaking R&D activities linked to at least one innovative project.[28] The proportion rose to 59.1 percent between 2004 and 2005, and just above half of those interviewed reported actual outcomes (56 per cent).[29] This important increase is, without doubt, related to the number of businesses with projects related to the bioequivalence and bioavailability sectors, with a view to accrediting generic medicines as interchangeable generic products.[30] Foreign firms carry out very little R&D and there seems to be no complementary work carried out between national and foreign companies. According to the Innovation Survey 2001, out of the total number of companies that carried out at least one innovative project, foreign companies accounted for 15 percent, while national companies registered the remaining 85 percent. Among the foreign companies, slightly over a third of them carried out R&D projects, while two-fifths of the national companies realized R&D projects. The percentage of turnover destined for R&D projects was very similar: 1.3 percent, in the case of multinational affiliated companies; meanwhile Mexican companies devoted 1 percent to this kind

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[28] Innovation Survey – 2001, INEGI-CONACYT, Mexico.

[29] Innovation Survey – 2005, INEGI-CONACYT, Mexico.

[30] A new reform relating to the registration of medicines in Mexico requires all companies to undertake studies to prove the bioequivalence and bioavailability of generics in order for them to be accredited as interchangeable generics through the COFEPRIS, otherwise they lose their registration.

of project. This percentage is relatively marginal when compared to the substantial proportion of turnover that the pharmaceutical corporations devote, in their own countries, to the discovery and development of new ingredients and/or new therapeutic uses for existing products (Guzmán and Brown, 2004).

To understand the nature of innovation in this industry, we focus on identifying what type of innovation was being carried out and in which fields. Considering that the Mexican pharmaceutical industry is not noted for its discovery and development of new molecules, the innovative activities are divided into those carried out by the multinationals and those undertaken by national companies. In the first case, the multinationals that reported innovative activities divided their efforts into two areas: on the one hand, the clinical development of new molecules, the first R&D stages having been carried out in their country of origin and, on the other hand, the clinical trials, the adaptation and introduction of the MNS pharmaceutical drugs into the local markets (galenic research). In the second case, the national companies in general concentrate their innovative activities on the development of generic products, once the patent on a molecule has expired. Linked to these activities, the companies adopt new processes and machinery allowing the conduct of bioequivalence and bioavailability tests for the generics. In only a few cases are local companies involved in the discovery of new molecules. In both cases we can refer to the innovations in products and processes, but in the majority of cases the innovations are incremental, given that they correspond to adaptations carried out on the original molecules for the local markets.

According to the Innovation Survey 2004–2005, the innovations introduced in the fields of production, and the organization of the pharmaceutical establishments that responded to the survey, were directed principally towards the introduction of radically new technologies (28.6 percent), the use of new materials (26.7 percent) and new production techniques (23 percent); of lesser importance were activities related to organizational innovations (5.7 percent) or new, professional *software* (0.5 percent). In relation to the products, 24.2 percent of the companies focussed on the introduction of new medicines, 28.8 percent on product improvements and 47 percent carried out no product improvements.

Weak technological development, insufficient human capital, and limited R&D has resulted in a low level of innovation and, therefore, a low rate of patents in the developing countries. In theory, the complementarity between internal R&D and the purchase of external technology transfer should generate a virtuous cycle for these companies. In industrialized countries, and some emerging East-Asian economies, the complementa-

rity between internal R&D and technology transfer has been associated with an increase in technological development and innovation (license and technical assistance agreements, and tacit knowledge transfer).[31] In the case of Mexico, contrary to studies on industrialized countries and other industries, the purchase of foreign technology has a marginal effect on the R&D activities of the pharmaceutical firms and their investment decisions (Zúñiga, Guzmán and Brown, 2007). In addition, R&D efforts do not affect the purchase of technology. The absence of a complementary relation may be explained by the divergence of the companies' technological objectives. While company R&D investment is explained by its participation in export markets, the purchase of technology is determined, above all, by capital intensity and the size of the company.

Next, we identify the main sources of external knowledge along with the internal R&D activities within the Mexican pharmaceutical industry. According to the Innovation Surveys, the expenditure on R&D activities in the pharmaceutical firms in Mexico constitutes the largest expenditure directed towards activities of innovation, and by 2005 this field received almost half of total investment. Second, in investment terms, was innovation-related expenditure on the purchase of machinery and equipment (the majority being imported), increasing from around a quarter of total investment in 2001, to 37.1 percent in 2005, indicating a process of modernization in the production of medicines. In addition, 8 percent of total investment in 2001, and 3.1 percent in 2005, was allocated to the acquisition of other external technologies, whether related to products or processes. Investment in industrial design and the introduction of new and improved production processes, activities clearly considered as endogenous innovation, or the adaptation of foreign technology, fell in 2005. Meanwhile, resources set aside for training programs amounted to 7 percent of total investment in 2001 and fell to less than half that in 2005. Finally, 9 percent was spent on the introduction of technological innovations into the markets. According to this data, the purchase of incorporated and unincorporated technology, probably foreign, represented around a third of the total expenditure dedicated to innovation in 2001, whilst in 2005 the figure was closer to two-fifths of total investment. See Figure 5.3. For a comparison with other Latin American countries, see Guzmán and Guzmán, 2009.

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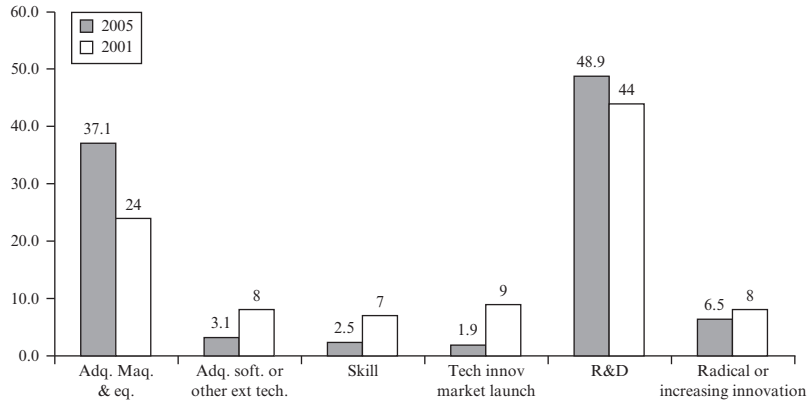
[31] See: Katrack (1994) and Lee (1996). In turn, the hard or incorporated technologies are those derived from the use of products (for example, machines, materials, and other production technologies) in which the technology can be dismantled with the help of technical manuals.



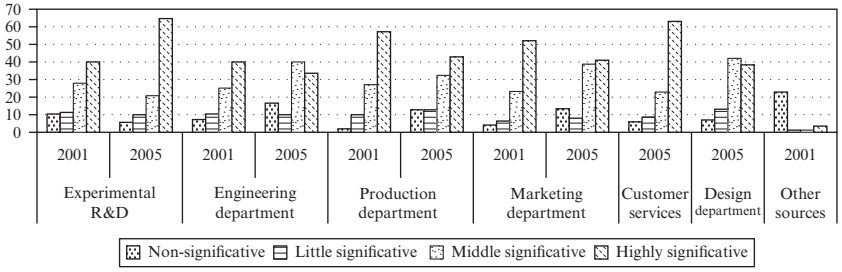
Source: Innovation Surveys, 2001, 2004–2005, Inegi-Conacyt, Mexico

Figure 5.3 Mexico – distribution of pharmaceutical firms' innovation expenditure, 2001–2005 (%).

Importance of R&D as an Internal Source of Technological Knowledge

Considering the crucial role played by R&D in the assimilation and generation of new knowledge, we can see the order of priorities chosen by the pharmaceutical companies vis-à-vis innovation in each and every activity they carry out (see Figure 5.4). In two fifths of these companies, R&D activities are highly significant; however, slightly over a fifth of companies regard the activity as insignificant, or slightly significant, and just 28 percent see it as moderately significant, in fact 12 percent of these companies do not even have an R&D department. A similar percentage of the companies attribute a high level of importance, moderate importance and slight importance to their engineering department, although the number of companies that consider this department as insignificant is lower, while those with no engineering department are higher in the overall percentage. As for the departments of production and marketing, over half the companies consider them highly relevant and very few consider them unimportant. Just 4 percent admit to having no production department, while 14 percent possess no marketing department. This suggests that companies concentrate their innovative actions on the fields of production and marketing, and is probably linked to imitative actions, whereby R&D and engineering departments play a much less significant role. The production of generic medicines would explain, in part, this type of company strategy.

The fact that almost two-thirds of the pharmaceutical companies in



Source: Innovation Surveys, 2001, 2005.

Figure 5.4 The importance of internal departments as a source of innovation in the Mexican pharmaceutical industry, 2001–2005 (%).

Mexico have no R&D departments suggests that this sector does not orient its activities towards innovation, and yet their imitative activities are limited, in the sense that there is no development of the capacities necessary for the efficient absorption of knowledge. Additionally, the absence of an R&D unit complicates the life of the companies in the marketplace due to the need for bioequivalence and bioavailability tests for registration with the COFEPRIS, following the newly introduced health regulations. Sixty-three percent have no R&D unit, while 37 per cent do.

External Sources of Technological Knowledge

A further aspect relevant to the analysis of R&D and innovative activities in Mexico's pharmaceutical sector concerns the importance of external sources of information technology (IT) (see Figure 5.5). This is reflected in companies' strategies on technological acquisition with regard to their imitative and innovative activities. The sources of information considered most important by these companies are: their clients (three-fifths of businessmen), equipment, material and components suppliers (over two-fifths), industrial fairs and expos (almost half), whilst their competitors play a role in two-thirds of the cases. This implies that it is market information to which the businessmen in the pharmaceutical industry attach the greatest importance with regard to the generation of new ideas. However, although low in number, there are firms who place great importance on patent activity (10 percent), universities and other higher education establishments (10 percent) and non-profit, public and private investigation institutions (5 percent), which reveals the significant distance that exists between the players in Mexico's pharmaceutical sector and the institutions that generate the new scientific knowledge and, to the same extent, frontier

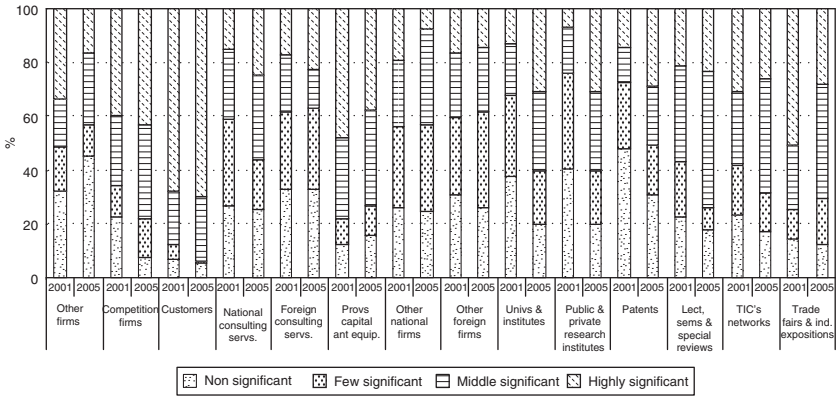


Figure 5.5 Importance of external sources of innovation in the Mexican pharmaceutical industry, 2000–2005 (%).

knowledge with regard to patent registration. Additionally, less than a third of companies consider that conferences, seminars and specialized magazines play a significant role in this field.

This low rate of interest in the information available in the field of patents, universities and institutions can be seen plainly in the fact that over half of the companies regard them as insignificant or of low significance. Other information sources, regarded by more than 50 percent of the companies as insignificant or of low significance, are those pertaining to national and international consulting companies, as well as other national and international companies in general. With regard to the importance placed on computerized information networks for innovative activities, the sector's businessmen have a heterogeneous opinion.

Finally, the financing for the development of innovation is of vital importance. Almost two-thirds of the companies which took part in the surveys said their R&D and innovation activities were self-financed; only a quarter received credits from the private banking sector, while 10 percent of the companies received financial help from subsidiaries or associated companies. It is striking that according to these surveys, there was an absence of help from governmental bodies, especially when considering that this is an industry requiring large amounts of investment.

Technology Transfer

Although there has been investment flowing into Mexico, there is no evidence that the local companies, in general, have taken into consideration

the area of technology transfer, nor have they made any real effort in the field of R&D. The cases in which local companies have applied a specific strategy with regard to technological innovation can be counted on the fingers of one hand, as can the links between companies and universities with a view to participation in the competitive environment, since the introduction of the NAFTA and the stringent IPR system (Guzmán and García, 2009).

There is a relative difference in the importance attached to the different fields with regard to contracts for technology transfers among the national and international companies. It is evident that the affiliated pharmaceuticals companies based in Mexico do not undertake substantial activities related to R&D; technology transfer is essentially orientated to brands, patents and technological assistance. Although national companies also focus their transfer efforts on the acquisition of brands, patents and technological assistance, the field of industrial design is dedicated to the development of R&D activities undertaken by national companies.

Cooperation between Universities and Companies

In Mexico, four-fifths of R&D activities are carried out in-house. When they are externalized, this is generally due to the fact that there is no in-house R&D laboratory, so these companies establish a cooperation agreement with an external research institute or another company. The ratio between the two is: 83 per cent in-house and 17 per cent external. Added to which, only a quarter of the pharmaceutical companies have an engineering department, the actual figures being 74 percent with no engineering department for R&D purposes and 26 percent with. Even if there is certain international recognition for Mexican researchers in the bio-pharmaceutical field and their publications in journals classified in the International Scientific Index (ISI), the knowledge generation capabilities in science are still relatively low. Furthermore, academic strengths in the production of scientific knowledge are not reflected in the business world (Guzmán and García, 2009) and there is a scarcity of links between universities and firms, mainly due to the absence of institutional policies regarding intellectual property and active technological transfer which would encourage technological cooperation between the two parties. In the academic sphere, researchers have sufficient incentives to publish, but not to patent. The few examples of collaboration between academics and industry do not usually take place through the institutional university channels, due to the fact that the legislation is still at an incipient level and promotion is lax.

Human Capital Specialization in the Pharmaceutical Sector

In the industrialized countries, the training of PhD students is the result of a joint effort between public and private sector companies, along with governmental organizations, thus strengthening the academic infrastructure of the universities and research institutions. As part of their professional activities, PhD students carry out research and development work in research institutes, engineering companies and laboratories; also, in the academic field, in universities and higher education establishments, with the formation of new human resources at the level of higher education in the fields of science and technology. The efforts made in Mexico in terms of PhD training are low compared to the industrialized and newly industrialized countries.[32] There is a significant level of backwardness with regard to the number of researchers per 1000 labor force (R/1000 lf). Mexico had 0.9 R/1000 lf in 2007, which contrasts with 9.2 in the US, 7.6 in France, 7.2 in Germany and 7.9 in Canada. Among the emerging countries Portugal had 7.2, China 2.0 and Turkey 2.1. Nevertheless, from 2000 to 2007 the number of PhD graduates in Mexico increased from 6.8 to 13.5 per 1000 people working in the fields of science and engineering (CONACYT, 2009). In 2008, two thirds of PhD graduates working in these fields were working in scientific fields linked to the pharmaceutical industry.

Scientific Publications and their Importance

According to the International Scientific Index (ISI) classifications, there are eight scientific disciplines linked to the pharmaceutical industry: molecular biology, biology, biotechnology, pharmacology, immunology, medicine, microbiology and neurosciences. On a global scale, Mexico has a low production of scientific publications. The greatest capabilities in Mexico are in the fields of microbiology and pharmacology. Despite Mexico's low number of international publications in the field of medicine, in the context of the country and, particularly, in the scientific areas of health and natural sciences, articles related to this discipline have the highest relative importance, followed by those of biology.

A further indicator of the importance of scientific output, measured in

[32] In 2001, the total number of researchers was divided mainly among the following geographical areas: Europe 34.3 percent, the United States 26.1 percent and Asia 33.3 percent. In the case of Asia, 13.7 percent were based in China. Meanwhile, Mexico contributed just 0.6 percent, even lower than Brazil, which was home to 1.3 percent of the total number of researchers.

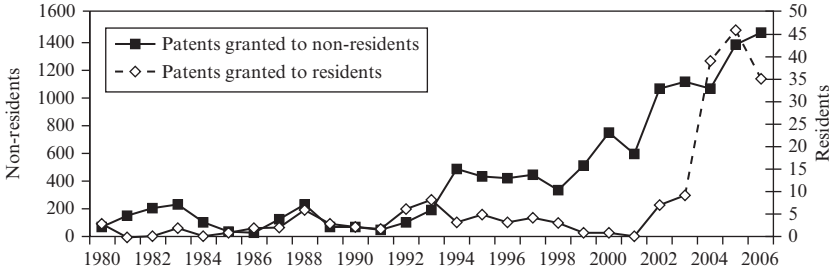
terms of publications, is the *impact factor*.[33] By studying this indicator, we can appreciate that the average number of citations received by publications in the case of Mexico in 1999–2003 was higher than other Latin American countries in the fields of molecular biology, immunology and pharmacology, thus revealing that scientific research of an international standard has developed in Mexico, and does have a relative impact.

INDUSTRIAL PERFORMANCE AND ACCESS TO DRUGS

National and Foreign Patenting in Local Offices of Intellectual Property in Mexico

In Mexico, after the approved IPR reforms of 1991, the number of patent applications in the pharmaceutical area in the local offices increased dramatically, rising from 239 applications in 1990 to 3,164 patents in 2006, with an average annual growth rate of 15.2 percent. Of the 11,936 patents granted in Mexico between 1980 and 2006, 98.4 percent were granted to non-residents and just 1.6 percent to Mexicans. Contrary to the trend in foreign patents, local patents have been marginal, although there was an increase from 3 patents in 1980 to 35 in 2006. Almost half of all the patents granted to non-residents in Mexico between 1980 and 2006 were to North Americans, predominantly in the United States; meanwhile, European companies were granted almost two fifths of the approved patents and Asia represented 7 percent of the total, with Latin America representing less than 1 percent. According to the patents consulted, we identified that 91 percent of the non-resident patent acquirers were companies, with institutions and individuals representing just 6 percent and 3 percent, respectively. Among the companies with the largest numbers of non-resident patents granted in Mexico are those from the US and United Kingdom, which are characterized as the leaders on a global level and/or have been the object of mergers or takeovers, such as Pfizer, Pharmacia, GlaxoSmithKline, Eli Lilly, Merck, Johnson, Abott and Bayer. The German companies Schering and Boehringer, the Swiss companies AstraZeneca and Novartis, along with the French company Sanof-Aventis, also play an important role in innovative projects. Almost half of the patents granted to Mexican residents were granted to individuals,

[33] The impact factor is defined as "the quotient between the citations and the number of articles in a determined time period" (CONACYT-INEGI, 2003, p. 70).



Source: IMPI (Industrial Property Mexican Institute), Banapa (National Bank of Patents). International class A61K.

Figure 5.6 Patents granted to residents and non-residents in Mexico by IMPI in pharmaceutical field, 1980–2006.

less than a third to companies and close to a quarter to institutions. See Figure 5.6.

Patents Applied for and Granted in the USPTO within the Pharmaceutical Field: the Diffusion Rate

The number of Mexican patents applied for and granted by the United States Patent and Trademark Office (USPTO) has been extremely low for the past three decades, which is linked to the lack of resources devoted to R&D in the national pharmaceutical industry.[34] The diffusion rate related to the inventive activity in Mexico's pharmaceutical sector is almost zero and remains practically at a standstill. The high cost of making patent applications to the USPTO or through the PCT[35] mechanism and the weak patent culture in Mexico are factors which undoubtedly affect the rate of diffusion of innovative activities in these countries.

On analyzing the patents granted in the pharmaceutical area with regard to the type of process and product, it becomes obvious that inno-

[34] Patents were consulted for the period 1980–2006 in this investigation from the USPTO in the classes 514 *Medicines and compounds for the treatment of bio-complaints of the body* and/or 424 *Drugs, bio-complaints and compounds for the treatment of the body*, for the pharmaceutical area. From the area of biotechnology, the consulted classes were 435 and/or 800. Considering that there are patents that can be in both classes of the USPTO, the search was carried out under the premise of *and/or*, so as to avoid duplication.

[35] By way of the PCT mechanism, the agents may patent in several countries simultaneously for a period of one year.

vative activity is present in both, although in the majority of cases we are talking about incremental innovations. Mexico has obtained several patents in the field of products.

In the pharmaceutical area (classes 514 and/or 424), Mexico has a reduced level of claims: 10.5 per patent. With regard to Mexican agents with patents in the pharmaceutical area, granted by the USPTO, companies obtained the patents in less than two-fifths of the cases, whilst institutions and individuals had a similar level (29 percent) of ownership of the patents.

Regarding the nationality of the patent inventors, in almost all cases, they are Mexicans. Of the 59 inventors registered in Mexico, only one is from the United States, two are from the European Union, and three are from other countries. The foreign participation in the patents granted in Mexico may be due to agreements made with institutions, or companies, but it could also be explained by the companies in question hiring foreigners for their research projects. One interesting experience is that of the company Probiomed, which, after taking the decision to substitute foreign technological transfer, then met obstacles in collaborating with national university researchers; they decided to hire foreign researchers.

The number of inventors per patent partly reveals the way in which new knowledge is produced, in the sense that it indicates the size of the R&D laboratories and thus the organization of the research teams. In countries which have accumulated technological capacities with a significant amount of activity in the R&D institutes, there has been a trend towards research teams becoming more consolidated. The patents in these countries are generally the result of joint research and, in a few cases, the result of one individual researcher. In Mexico, there is participation of between 5 and 10 researchers in the invention area of the pharmaceutical sector.

Access to Medicines

From the point of view of some local firms, Mexico has always been a market where new world pharmaceutical products were introduced without delay, later followed by the generic versions, either through licensing of the patent or by means of reverse-engineering, during the period of lax patenting.[36] Nevertheless, the speed of Mexican firms' imitation capabilities was an important argument against the introduction of some new drugs. Consequently, American MNS pharmaceutical firms were

[36] This is the case for Ranicen by Glaxo, a generic version of which was produced very rapidly by Senosian, a Mexican firm.

instrumental in lobbying for the strengthening of IPR and especially the patent system in Mexico, prior to the NAFTA negotiations. Since 1991, the IMPI has registered an important growth in the number of foreign patent applications and patents granted. We deduce from the adoption of the TRIPS and the significant increase in patents applied for and granted that these firms had great expectations of introducing new medicines to Mexico under this new IPR environment. Therefore, the strong patent system seems to have favored the availability of new generation medicines in Mexico's pharmaceutical market. On the other hand, it has destroyed the possibility to introduce generic versions into the Mexican market, to the detriment of those involved in the procurement of medicines.

In 2009, almost half of the population receiving medical coverage through the IMSS and the ISSSTE had regular access to the prescription of medicines for the treatment of diseases and for other medical interventions. A further 45 percent of the population could access the medicines through other state or federal services, including Popular Health Insurance, and 5 percent by private means (IMS, 2010).[37] However, each social security service has its budget constraints; each has its own structured procedure to purchase medicines according to medical priorities. In the case of the SPS, this depends on the established guidelines and the financial capacity of the Ministry of Health. The expenditure of the public health institutions on medicines and medical inputs grew 60 percent between 2004 and 2010 (this last year is estimated). Although the budget allocated to drug procurement is higher, the affiliates do not always satisfy their needs completely from the institution and they must buy out of their own resources. As we have seen, the financial resources for purchasing medicines have increased as regards patented medicines, but with fewer units, and on the other hand, the share of the budget used for generics has decreased. Moreover, the deep problems of financial sustainability of the public health institutions and the regulations restricting the introduction of generics onto the market (associated with the drug approval procedures, as explained above), make it more difficult to assure the entire coverage of medicines needed by patients. As a consequence, for some illnesses, such as HIV/AIDS, the coverage of antiretrovirals (ARV) is almost complete – between 82 and 95 percent (CENSIDA-SS, 2010), but for other kinds of disease there are occasionally shortages or delays in supplies.

[37] According to the Health Law Reform (10 April 2007), 30 million people did not have access to medicines, 55 million had access through IMSS and ISSSTE and 15 million could have private consultations and purchased the medicines on their own. Only three percent of the Mexican population has private health insurance (Moïse & Docteur, 2007).

When patients have to follow a treatment without interruption, they will be forced to buy the medicines themselves in the private market or wait until the medicine becomes available again in the institution.

Of the total expenditure on medicines in Mexico in 2009, 64.7 percent was out-of-pocket, 2.4 per cent was from the private sector and one third from the public health institutions (17 percent from the IMSS, 6 percent from the ISSSTE and 10.2 percent from the Ministry of Health and SSP).

Prices

Historically, drug prices in Mexico have been lower than in other OECD countries.[38] In 1987, both the consumer prices index (CPI) and pharmaceutical consumer price index (PCPI) recorded inflation of three digits (more than 180 and 160 percent, respectively), which fell to two digits in 1988. From 1988 to 1990 the CPI rose faster than the PCPI. From 1991 (when Mexico adopted the stringent IPR reforms) to 1999 the price indexes on pharmaceutical products were higher than those of the CPI, following a policy of price flexibility. Since September 1996, there has been an agreement to regulate the prices of medicines by adopting the maximum-price regulation.

An analysis by the Ministry of Health (2002) found that in more than 43 percent of cases the retail sale prices were higher than maximum permitted retail prices (González-Pier and Gonzalez 2004). Therefore, in 2004, maximum price regulation was adopted. The pricing agreement was signed jointly by the Ministry of Economy and CANIFARMA (representing the members of AMIIF). The main points of this reform, administered by the Ministry of Health, are: i) the regulation applies only to patented medicines on the private market; ii) the manufacturers' participation is voluntary; iii) the international prices are taken as a reference to establish the maximum retail sales price; iv) in the case of new products, the manufacturers fix the prices, which can be re-evaluated three months after product launch; v) generic products and original products whose patents have expired are not considered for price regulation; vi) three different prices are considered in the price regulation: the international reference price; the reference price for retail sales and the maximum retail sales price.

As a consequence, PCPI inflation has slowed down to one digit since 2004, reaching the lowest figure in 2008 (2.7 percent) and low than the

[38] In the early 1990s, prices of pharmaceutical products in Mexico were 5 times lower than in the United States and 3 times lower than in European countries (IMS Health, 2005, cited in Moïse and Docteur, 2007).

pharmaceutical producer price index (PPPI) (5 percent). The next year (2009), the producer price index remained higher than the consumer price index. A new study was conducted in 2005, revealing that in 73 percent of cases the maximum price of the 273 medicines in the sample was lower than the international reference price and in 2 percent of cases were equivalent. Another study on comparative pharmaceutical prices (Danzón and Furukawa, 2003) showed that Mexican prices in this sector were 80 percent of those in the United States and were lower than in Germany, Italy and the United Kingdom, but higher than in Canada and France. Generic prices in Mexico were higher than in the United States and patented medicine prices were lower. Commenting on these findings, Danzón and Furukawa underline that Mexicans pay higher prices if we take into account the comparative income level. The lower per capita income level of the country is probably not the only reason for the price elasticity of demand. Other factors that should be considered include income distribution preferences and the level of out-of-pocket payments for pharmaceutical purchases.

In the case of the public sector, the consumer price index figures of the basic listing medicines have significantly decreased, falling from 3.68 in 2004 to –24.5 in 2009. Meanwhile, private sector prices and the consumer price index recorded a high increase, with an important divergent trend.

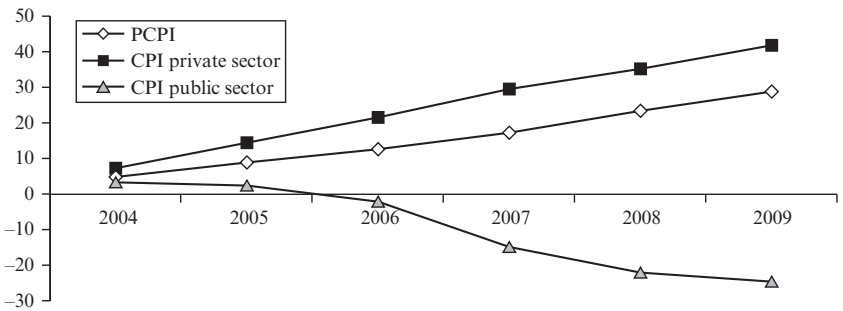
Among the medicines in the public sector, the prices of some therapeutic classes fell on average between 2003 and 2009, probably linked to the introduction of more generics, although some patented medicines have been also included in the public sector. This was the case for ophthalmology (–79.1 percent), cardiology (–42.30), psychiatry (–38.02), infectious diseases (–18.11), gastrointestinal diseases (–11.89) and neurology (–0.27).[39] Otherwise, in the same period, the prices of other therapeutic classes of medicines have risen on average as follows: nutrition (45.33 percent), rheumatology (37.40), dermatology (11.16) and otolaryngology (4.9). The high inflation here suggests the existence of patented products.

The role played by Simi medicines, i.e. non-bioequivalent or 'similar' generics, up until 2010 gave many people the opportunity to access drugs at hugely reduced prices, especially the lowest income and uninsured people. The lower people's income the higher is their propensity to buy Simi generics (IIIFAC). From 2003 to 2008, the sales of Simi pharmaceu-

[39] Sources: Pharmaceutical and Medical National Institute of the Public Sector – INEFAMSP, Spanish acronym of Instituto Nacional Farmacéutico y Médico del Sector Público; Pharmaceutical Research Institute – IIIFAC, Spanish acronym of Instituto Farmacéutico, A.C.

Source: Pharmaceutical Research and Innovation Institute, A.C., with Banxico and INEGI database.

Figure 5.7 Consumer and producer prices index in drugs market in Mexico, 2000–2009.



Source: Pharmaceutical Research and Innovation Institute, A.C., with Banxico and INEGI database.

Figure 5.8 Accumulated inflation of the consumer, public and private sector of the basic listing of medicines in Mexico, 2004–2009.

tical products almost doubled in terms of units; basically they are inferior goods and the lower prices are also due to the fact that Simi has its own distribution chain of pharmacies throughout the whole country and they import low-price inputs from India and China, among other countries. As Simi products have increased their presence in the pharmaceutical market, their sales growth has fallen. After concentrating on the bioequivalence test to obtain marketing approval from the COFEPRIS, the Simi generics producers are now seeking to introduce products in new therapeutic classes and to bid in the public sector.

Another recent competitor in the pharmaceutical market is Walmart. The chain of Walmart supermarkets has become a leader in its own brands of pharmaceutical products. In 2007, it introduced 150 medicines and in March 2009 it sold 457 drugs, and their suppliers have risen from 14 to 28 laboratories. Their prices are 50 percent lower than those of other leading products.

CONCLUSIONS

The technological efforts in Mexico's pharmaceutical sector are still relatively low. Companies are still reluctant to assume the costs of R&D and of developing their own patents, considering it unnecessary. Although local companies have been forced to modernize and undertake the necessary tests, so as to have their interchangeable generic medicines approved, there are still very few that have increased their efforts in the areas of discovery, research and the development of new pharmaceuticals. The scarce resources dedicated to R&D activities are still focused on the imitative strategy, that is to say, on the exploitation of expired medical patents.

Mexico is still low down the international ranking in terms of its capacity to generate scientific knowledge, despite relative international acknowledgement for the publications produced by the scientific community in the fields related to bio-pharmaceuticals. However, this strength in the academic fields is not necessarily reflected in the realm of business. This reveals the absence, or at least weakness, of the connections between companies, universities and research institutions. Awareness of the importance of the links between business and universities has led to some successful cases. Alliances between companies are also scarce, which results in the work carried out by some companies being somewhat fragmented. Companies have had to organize themselves in the face of adverse economic policies, but this kind of organization has been lacking with respect to R&D projects.

Regarding the innovation model, in terms of the players that dominate the market, technological efforts and domination in the systems of intellectual property, we found that the pharmaceutical sector in Mexico is dominated by a multinational model; not because of the foreign companies spreading their technological and innovative efforts throughout the country, but rather because they have increased their control over the national market and have thus been the beneficiaries of the patent system, while local companies and institutions have made weaker technological and innovative efforts, thus leading to a limited level of market participation.

The type of patent system is characterized as being divergent. In effect, there is a high relative dependence, which implies that a greater number of foreign (non-resident) patents are being applied for at the local offices, when compared with the number of national (resident) applicants. In addition, the inventive coefficient level (patents per million inhabitants) is marginal. This suggests that the new technological knowledge (pharmaceutical products and processes) that is protected belongs to foreigners and, as a result, the beneficiaries of the monopolistic exploitation related to patents also remains in the hands of the foreign companies (multinational companies, in most cases).

Mexico's adoption of the TRIPS, in a context of meager economic growth, recurring economic and political crises and unfinished institutional changes, in conjunction with low levels of investment in R&D activities, does not provide any incentives to participate in innovation projects. These factors result in a status quo with regard to the low number of patents granted per year in comparison with the Asian countries. The adoption of the TRIPS in Mexico has favored the multinational companies, because the opportunities open to national companies are limited by their low capacity for imitative and innovative projects, concentrated in just a few local companies which have been able to develop some niche opportunities.

Given the strategic importance of the pharmaceutical industry in the health and well-being of the population, Mexico should strengthen this industry, focusing on innovation in specialized areas, whilst at the same time developing the country's capabilities in the production of interchangeable generic products. Good competitive performance also involves an improvement in the commercial balance, efficiency in public health policies and an increase in the scale of the knowledge-based economy. In recognition of the crucial importance of R&D and innovative activities, within an adequate macro, micro and institutional environment, Mexico must take up the challenge to achieve a modern and competitive industry, requiring the design of industrial, fiscal, financial and educational policies to allow the development and accumulation of technological capacities.

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