

# Pharmaceutical Innovation, Incremental Patenting and Compulsory Licensing

Editor  
Carlos M. Correa



  
**SOUTH  
CENTRE**

**PHARMACEUTICAL INNOVATION, INCREMENTAL  
PATENTING AND COMPULSORY LICENSING**

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Carlos M. Correa



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## CONTRIBUTORS

**Tahir Amin** is the Co-Founder of I-MAK and Director of Intellectual Property. Tahir is a practising solicitor of the Senior Courts of England and Wales and has 15 years' experience with two of the leading IP firms in the UK and as an in-house global IP manager for a multinational company. Tahir's experience covers prosecuting, licensing, opposing and litigating trademarks, patents, and designs. Prior to founding I-MAK, he spent two years in India researching public interest IP issues and working on pharmaceutical patent oppositions. He has served as legal advisor/consultant to many organisations, including the World Health Organization, UNITAID, Clinton Foundation HIV/AIDS Initiative, GAVI, Doctors without Borders and Oxfam. Tahir has published in many prominent fora including Health Affairs, Nature Biotechnology and Science. Tahir was formerly a Fellow at the Harvard Medical School in the Department of Global Health & Social Medicine.

**Dr. Carlos Maria Correa** is Special Advisor on Intellectual Property and Trade of the South Centre and Director of the Center for Interdisciplinary Studies on Industrial Property at the Law Faculty, University of Buenos Aires. He has been a visiting professor in post-graduate courses of several universities and consultant to UNCTAD, UNIDO, UNDP, WHO, FAO, IDB, INTAL, World Bank, SELA, ECLA, and other regional and international organizations. He has advised several governments on intellectual property, innovation policy and public health. He was a member of the UK Commission on Intellectual Property, of the Commission on Intellectual Property, Innovation and Public Health established by the World Health Assembly and of the FAO Panel of Eminent Experts on Ethics in Food and Agriculture. He is the author of several books and numerous articles.

**Gabriela Costa Chaves** is a pharmacist, holds a Masters in Public Health and is a PhD candidate (2011) in Public Health in the Sergio Arouca National School of Public Health (ENSP), Fundação Oswaldo Cruz (Fiocruz). She was a Junior Researcher in the Center for Pharmaceutical Policies ENSP/Fiocruz (2002-2006), and also a member

of the secretariat of the Rebrip's Working Group on Intellectual Property (GTPI/Rebrip) in the Brazilian Interdisciplinary Aids Association (2006-2008). She represented Médecins Sans Frontières' Access Campaign in Brazil from 2006 to 2011.

**Arti Malik** has been working as an advocate and researcher for the past 7 years with a focus on human rights, law and public health. She has worked on health policy reform in India with a specific experience on HIV/AIDS, access to medicines and maternal and child health. She has a background in law and holds a Master's degree in health promotion and international development from the University of London.

**Priti Radhakrishnan** is Co-Founder and Director of Treatment Access of I-MAK. Priti obtained her law degree from New York University (NYU) School of Law and has worked as a health attorney in the U.S., Switzerland and India. Prior to founding I-MAK, she served as the Senior Project Officer of the Lawyers Collective HIV/AIDS Unit in India. In 2008, Priti was awarded the Echoing Green Fellowship for social entrepreneurs and the Pop!Tech Social Innovation Fellowship. The Asia Society recently selected Priti as one of three young leaders from the United States for its 2009 Class of Asia 21 Fellows and a 2011 Associate Fellow. Priti was awarded the 2010 Black, Latino, Asian Pacific American NYU Law Association's Young Alumni Award, named NYU School of Law's Alumnus of the Month (November 2009) and was the 2010 Honoree of the NYU Law Women of Color Collective. Priti was recently selected by the King Baudouin Foundation as one of a group of young visionaries making change for its Spotlight on the Millennials series. In 2012 she served as a Mentor at the Unreasonable Institute, an international accelerator for high-impact entrepreneurs and a recipient of the South Asian Bar Association of New York's Legal Trailblazer Award. Priti is currently an adjunct faculty member at the St. Luke Foundation/Kilimanjaro School of Pharmacy.

**Renata Reis** is a journalist and lawyer. She is a Ph.D. candidate in Public Policy, Strategy and Development at the Institute of Economics of the Federal University of Rio de Janeiro – UFRJ. She holds a Masters in Social Policy from the State University of North Fluminense Darcy Ribeiro - UENF (2005) with part of the course at the Free University of Brussels - ULB, Belgium. Renata is an expert on intellectual property at Fundação Getúlio Vargas. She worked seven years at the Brazilian Interdisciplinary AIDS Association and was Coordinator of the Working Group on Intellectual Property Rights – GTPI during this period. Renata currently works on institutional relations with Médecins Sans Frontières - Brazil. She is also a fellow at the Institute for Applied Economic Research - IPEA, and is the legal counsel. She is a member of the Bioethics and Biolaw, the OAB-RJ. Author of "Patents and Industrial Creations", published by Fundação Getúlio Vargas Press, Renata is also the author of several articles and is responsible for organizing publications in the field of access to medicines.

**Dr. Padmashree Gehl Sampath** is a well-known international expert on innovation and development issues, currently working at the United Nations Conference on Trade and Development (UNCTAD) in Geneva as Chief of the Technology and Innovation Report Series. Prior to this, she worked for several years as a Researcher at the United Nations University-MERIT (2002-2007) and then as an Assistant Professor on International Development and Innovation at the Open University, UK (2007-2008). She has a research specialization in innovation and development economics, and has contributed extensively to international and regional debates on issues of innovation, technology and development issues through research results from the various projects that she has led in the field. She has an extensive publications record, including several journal publications, chapters in books and four published books. Dr. Gehl Sampath has received awards for her accomplishments from the Rockefeller Foundation in 2009 and more recently, the Rotary International in India for ‘Outstanding Achievements’ in 2010.



**Francisco Rossi** is a Physician and Epidemiologist with more than 20 years of national and international experience in public health, health reforms and regulatory issues particularly in pharmaceuticals. He is an international consultant for the World Health Organization (Equatorial Guinea), Pan American Health Organization (Ecuador, Peru, Bolivia, Guatemala, Nicaragua, Dominican Republic, Honduras), Inter-American Development Bank (Argentina, Paraguay), World Bank (Nicaragua) and the European Union (Nicaragua) on pharmaceutical policies. Francisco was the General Director of Medicines Regulation at the Colombian Ministry of Health during 1990. He also acted as PAHO adviser for the regulation of medicines during the Colombian health reform (Law 100-1993) and International Adviser at PAHO for the National Programme of Essential Medicines in Bolivia from 1996-2000. Francisco was also Adviser for the Minister of Social Protection of Colombia for the national pharmaceutical policy in 2003. He was Coordinator of the IP and access to HIV medicines project at UNDP in Brasilia, Brazil from 2004-2007. Francisco is the current Director of IFARMA Foundation, since 2007.

**Yousuf A Vawda** is an Associate Professor at the University of Kwa-Zulu Natal (UKZN) School of Law, Durban, South Africa, and holds the academic qualifications BA, BProc, LLM and an LLD which he obtained at UKZN with his doctoral thesis entitled “Access to Life-saving Medication in South Africa: The Case for Legislative Reform”. Yousuf is admitted as an Attorney of the High Court, South Africa, served as Director of the Law Clinic, University of Durban-Westville, and now serves as Academic Leader: Public Law at UKZN’s School of Law. He has been actively involved in the community for more than 30 years providing legal advice and support to various community organisations including civic, political, professional bodies and other civil society groups. Yousuf holds positions on various boards such as the Board of Directors – Legal Aid South Africa, and is a founding trustee of the Association of University Legal Aid Clinics (AULAI) Trust. Yousuf’s research interests lie in access to justice and access to medicines issues. He teaches courses in Professional Training, HIV/AIDS Human Rights & the Law, and Intellectual Property & Access to Medicines, and has published in these areas. He may be contacted at: [vawday@ukzn.ac.za](mailto:vawday@ukzn.ac.za).

## ABBREVIATIONS

ABDI	Brazilian Agency for Industrial Development
ACEMI	Colombian Association of Insurers (Asociación Colombiana de Empresas de Medicina)
ADI	Direct Action of Unconstitutionality
AFIDRO	Association of Research-based Pharmaceutical Laboratories in Colombia (Asociación de Laboratorios Farmacéuticos de Investigación y Desarrollo)
AGU	Brazilian Attorney General
ANDI	Colombian National Association of Industry (Asociación Nacional de Industriales de Colombia)
ANMAT	National Drug, Food and Medical Technology Administration
ANVISA	Brazilian Health Surveillance Agency
API	Active Pharmaceutical Ingredient
ARV	Antiretroviral
ATPDEA	Andean Trade Promotion and Drug Eradication Act
BID	Inter-American Development Bank
BNDES	National Bank of Economic and Social Development
CAN	Andean Community of Nations (Comunidad Andina)
CAPES	Coordination for the Improvement of Higher Education Personnel
CEDIN	Documentation and Technological Information Centre of the Brazilian Patent Office
CIDE	Contribution of Intervention in the Economic Domain
CIPRO	Companies and Intellectual Property Registration Office (a division within South African Department of Trade and Industries)
CIS	Industrial Health Complex
CNPM	National Price Commission for Medicines (Comisión Nacional de Precios de Medicamentos)
CNPq	National Council for Scientific and Technological Development
CNS	National Health Council
CNSSS	National Council on Social Security for Health (Consejo Nacional de Seguridad Social en Salud)
CODETEC	Company of Technological Development

CPCC	National Civil and Commercial Procedural Code
CPI	Industrial Property Code
CUP	Paris Convention
DANE	National Department of Statistics (Departamento Administrativo Nacional de Estadísticas)
DCB	Brazilian Non-proprietary Name
DIAN	National Revenue and Customs Agency (Dirección de Impuestos y Aduanas Nacionales)
DRA	Drug Regulatory Authority
DSB	Dispute Settlement Body (of the WTO)
DSU	Dispute Settlement Understanding
ECOPETROL	Colombian Petroleum Company (Empresa Colombiana de Petróleos)
EFTA	European Free Trade Agreement
ESE	State Social Enterprise (Empresa Social del Estado)
FDA	Food and Drug Administration
FFAA	Armed Forces (Fuerzas Armadas)
FINEP	Research and Project Financing
FNDCT	National Fund for Scientific and Technological Development
FOSYGA	Solidarity and Security Fund (Fondo de Solidaridad y Garantías)
FS	Sector Funds
FTA	Free Trade Agreement
GATT	General Agreement on Tariffs and Trade
GDP	Gross Domestic Product
GIPI	Inter-Ministerial Group on Intellectual Property
GMP	Good manufacturing practices
HAI	Health Action International
HH Index	Herfindahl Hirschman Index
IBGE	Brazilian Institute of Geography and Statistics
ICTs	Institutions of Science and Technology
ICTSD	International Centre for Trade and Sustainable Development
IMS	Intercontinental Marketing Services
INN	International Nonproprietary Name
INPI	National Institute of Industrial Property
INVIMA	National Regulatory Agency (Instituto Nacional de Vigilancia de Medicamentos y Alimentos)

IPI	Industrialized Products Tax
IPS	Health Services Provider Institution (Institución Prestadora de Servicios de Salud)
LIT	Law of Technological Innovation
LPI	Brazilian Industrial Property Law
M.E.y O.y S.P.	Ministry of Economy and Public Works and Services
M.S. y A.S.	Ministry of Health and Social Assistance
MCC	South Africa's Medicines Control Council
MCT	Ministry of Science and Technology
MDIC	Ministry of Development, Industry and Foreign Trade
MoH	Ministry of Health
MPS	Ministry of Social Protection (Ministerio de la Protección Social)
MS	Ministry of Health
NEML	National Essential Medicines List
NPP	National Pharmaceutical Policy
OECD	Organization for Economic Cooperation and Development
OTC	Over the Counter
PCT	Patent Cooperation Treaty
PFTB	The Brazilian Popular Pharmacy Programme
PhRMA	The Pharmaceutical Research and Manufacturers of America
PITCE	Industrial, Technological and Foreign Trade Policy of the Federal Government
PMOE	Compulsory Emergency Medical Programme
PNCTIS	National Policy for Science, Technology and Innovation in Health
PNM	National Medicines Policy
POF	Family Budget Research
POS	Compulsory Health Plan (Plan Obligatorio de Salud)
PROFARMA	Support Programme for the Development of the Pharmaceutical Productive Chain
R&D	Research and Development
RENAME	National List of Essential Medicines
SACU	Southern African Customs Union
S&T	Science and Technology
SGSSS	General System of Social Security in Health (Sistema General de Seguridad Social en Salud)

SIC	Superintendency of Industry and Commerce
ST&I	Science, Technology and Innovation
STF	Brazilian Supreme Court
SUS	Unified Health System
TAC	Treatment Action Campaign
TDF	Tenofovir disoproxil fumarate
TPA	Andean Trade Preference Act
TRF	Regional Federal Court
TRIPS	Agreement on Trade-Related Aspects of Intellectual Property Rights
TRIPS	Trade-Related Aspects of Intellectual Property Rights
UNCTAD	United Nations Conference on Trade and Development
UNDP	United Nations Development Programme
UPC	Per-capita unit of payment (Unidad de Pago por Capitación)
USTR	United States Trade Representative
WHO	World Health Organization
WTO	World Trade Organization

# CHAPTER 1

## PHARMACEUTICAL INNOVATION, INCREMENTAL PATENTING AND COMPULSORY LICENSING<sup>1</sup>

Carlos M. Correa

### I INTRODUCTION

The patent system was devised in order to reward inventiveness, encourage technical progress and foster the dissemination of innovations. The restriction to the free movement of ideas that the granting of a patent entails has been justified under different theories, namely natural rights, moral reward, incentive to invention, encouragement to innovation. The idea that patents are necessary to allow the investor to recoup its investment in Research and Development (R&D) dominates in current debates and jurisprudence of many countries (Guterman, 1997).

Although the development and exploitation of numerous contributions to technology have been closely linked to, although not necessarily determined by, the possibility of obtaining exclusive rights to exploit inventions (Archibugi and Malaman, 1991), the patenting system is far today from fulfilling its intended objectives. The expansion of the subject matter of patentability from inanimate to living forms, the admission of broad claims encompassing vast fields of technology, the dilution of the patentability requirements, and shortcomings in the examination process, have led to a profound distortion of the system (Jaffe and Lerner, 2004). There is a proliferation of patent applications and grants, in great part motivated by a variety of defensive and offensive patenting strategies (Granstrand, 1999).

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<sup>1</sup> This chapter summarizes the findings of the research conducted with the support of the International Development Research Centre (IDRC, Project No. 105168), whose outcomes are presented in this book.

One increasingly widespread view is that the role of the patent system in promoting innovation is less substantial than usually claimed (Landes and Posner, 2003; Levin et al., 1987). Patents may even stifle the very innovation they are supposed to foster (Jaffe and Lerner, 2004). There is compelling evidence indicating that ‘collective invention’ based on sharing innovations is more efficient than patenting them (Bessen and Meurer, 2008); some studies suggest that innovation not only thrives in a competitive environment, but that more profit can be generated by inventors in a system based on the broad diffusion and common use and improvement on innovations (Torrance and Tomlinson, 2009).

The large number of patents applied for and granted is not a reliable indicator of innovation. While the number of patent applications and grants has increased dramatically, notably in the United States of America but in other countries as well,<sup>2</sup> this growth is not caused mainly by a surge in R&D spending (Bessen and Meurer, 2008, p. 69). One of the probable causes of such a surge in some jurisdictions is the relaxation of patent requirements by patent offices and courts. The National Academies of the United States, for instance, have taken up the criticism levelled by many academics and sectors of industry and have expressed their concern about the lax application of the patentability standards (National Academies of Science, 2003), especially as regards non-obviousness and usefulness, in the examination and granting of patents. The application of such standards result in many over-broad (Mazzoleni and Nelson, 1998) or “low quality” patents (FTC, 2003). In the case of the USA, it has been found that an inadequate search of previous patents and publications leads patent examiners to overlook novelty and inventive step problems; in addition, courts have shown a proclivity to weaken the obviousness test (Bessen and Meurer, 2008). Even the users and main beneficiaries of the patent system have become growingly critical about the functioning of the patent system.<sup>3</sup>

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<sup>2</sup> China's State Intellectual Property Office (SIPO) received a record 1.2 million patent applications during calendar year 2010, a 25 per cent jump on the 2009 figure. See Quality is China's biggest patent challenge – available from <http://www.iam-magazine.com/blog/Detail.aspx?g=e81c5421-bccc-4eb5-9895-f347443cf73e>.

<sup>3</sup> A survey conducted among large companies (with annual revenues exceeding US\$10 billion) by the Intellectual Property Owners association (IPO) in August

Patents are not granted only when a significant technical development has been achieved. Inventions marked with considerable originality (Merges and Nelson, 1996, p. 128) do not occur frequently, even in highly intensive R&D industries. In fact, the largest part of R&D undertaken (by large and small firms) is devoted to the improvement on and further refinement of existing technologies. Although not all types of incremental innovations may be eligible for patent protection, many actually do. According to a Guide of the Canadian Intellectual Property Office, for instance, 90 per cent of all patented inventions were minor improvements on existing patented devices (Canadian Intellectual Property Office, 1994).

As incremental innovations prevail in most sectors, the patent system has increasingly moved away from its objective of stimulating genuine invention towards a system for the protection of investment in developing incremental innovations, whether truly inventive or not. As a result, for some analysts, “the time has come not for marginal changes but for wide-open thinking about designing a new system from the ground up” (Thurow, 1997). In fact, an optimal level of patent protection beyond which negative effects would start to dominate positive effects is likely to exist (Guellec, 2007, p. 73). Patents produce a dead weight burden insofar as the benefits of innovations to society would have been greater in their absence, while they reduce the ability of other firms to exploit innovations on a competitive basis (Maskus, 1997, p. 3). The latter is a critical problem in the case of cumulative systems of technology, where patents may deter rather than promote follow-on innovations.

Patents are granted to promote innovation. The formulation of a patent regime, hence, should not be dissociated from the characteristics

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2005 showed that its corporate members perceive the quality of patents granted by the US patent and trademark office to be less than satisfactory. Over half of respondents, 51.3 per cent, rated the quality of patents issued in the US today as less than satisfactory or poor (47.5 per cent less than satisfactory and 3.8 per cent poor). Those rating quality more than satisfactory or outstanding were 8.8 per cent of all respondents (8.8 per cent more than satisfactory and 0 per cent outstanding). Respondents' prognosis for the future was not encouraging. Over two-thirds of respondents said they would be spending more, not less, on patent litigation over the coming years (*PR Newswire*, 2005).



of the national innovation system<sup>4</sup> of the country where such regime applies. In most developing countries the innovation systems are fragmented and weak, and they overwhelmingly depend on foreign innovations. In many developing countries the public sector modestly invest in scientific activities - generally focused on subjects of research of interest to developed countries- while domestic firms generate “minor” or “incremental” innovations largely derived from the routine exploitation of existing technologies. Domestic firms generally follow “imitative” or “dependent” technological strategies, usually relying on external sources of innovation, such as suppliers, customers and competitors.

However, there are growing differences among developing countries. Some developing countries (such as China, Brazil and India) that are more scientifically advanced than others are starting to reap benefits from decades of investments in education, research infrastructure, and manufacturing capacity. These countries, which have been called in recent literature as ‘innovative developing countries’ (IDCs) (Morel et al., 2005, p. 401), invest in R&D relatively more than other developing countries, there is a greater involvement of the private sector, and the interactions between public institutions or private companies with innovation agents in developed countries are more frequent.

Adapting the patent regime to different innovation systems is not a simple task. The considerations relevant to an IDC may well be different from those relevant to less technologically advanced countries. These differences, however, should not be overstated since, on the one hand, developing countries, including IDCs are equally vulnerable to patent strategies of large companies from developed countries and, on the other, a large portion of the population in those countries live in poverty, and will equally bear the costs of tight patent regimes in terms of reduced access to essential goods, such as medicines and chemical products for agriculture.

A key question is how to frame a patent regime in a country where the innovation path is centred on minor/incremental technical

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<sup>4</sup> See, on this concept, Lundvall, 1992.

changes. At first sight, such innovations may be regarded as outside the patent system and a different set of measures (such as utility models) to promote them would seem to be called for. It has been argued, however, that a patent regime based on a low inventive threshold could be functional to the predominantly incremental innovation path prevailing in developing countries, as patents might encourage minor innovations developed by domestic companies. In accordance with this view, the possibility of patenting minor innovations may encourage such companies to improve on existing technologies.

This expansive approach on inventive step, however, may have negative consequences. On the one hand, large firms with experienced teams of patent lawyers are much better prepared, financially and technically, than domestic firms to exploit a patent regime with a low patentability threshold; there is a risk of blocking innovation and competition, rather than promoting it. In addition, the public will be bound to pay monopoly prices for access to knowledge and products that should be in the public domain.

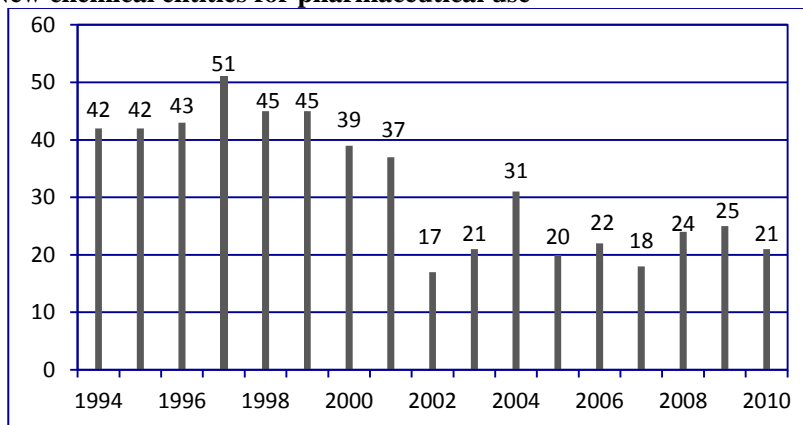
On the other, the cost of acquisition and, particularly, exercise of patent rights is too high for most local innovators, generally small and medium enterprises (SMEs). While SMEs could opt in many cases to seek patent protection, they must bear the costs of filing, registration and maintenance. If there is litigation (either to enforce the patent against infringers or to defend it from validity challenges) victory in courts is not assured, damage claims by counterparts may be high and litigation costs may be prohibitive. A report on the impact of patents on SMEs in the United Kingdom, for instance, found that “the use of patents as a means to construct and protect proprietary know-how is not the preferred choice of firms”. Despite much emphasis on patents both in the economic literature and in the policy debate, secrecy and lead-time advantages seem to be much more important and this is especially so for smaller firms... Patents could in principle be used as learning inputs by firms seeking to monitor and/or imitate their competitors’ innovative behaviours. However, this function does not appear to be especially important, least of all for SMEs (Hughes and Mina, 2010).

The problems associated to the patenting of minor incremental developments have special implications in the case of pharmaceuticals

necessary to protect public health. Patents on pharmaceutical products and processes may be used to block generic competition that lower prices and enhances access to medicines, particularly by the poor. This may be the case even when the original patent on a medicine has expired and the drug is in the public domain. Patents relating to a known compound (e.g. new formulations, dosages, crystal forms, etc.) are often strategically used to exclude competitors from the market.<sup>5</sup>

While the number of new-developed chemical entities has dramatically fallen during the last fifteen years (see Figure 1), the number of patents over simple changes in chemistry/formulation of existing pharmaceutical products (e.g. polymorphs, combinations, dosage forms, isomers) has continuously increased. Thousands of patents are granted per year on these incremental innovations, often trivial for a person skilled in pharmaceutical research and production.

Figure 1

**New chemical entities for pharmaceutical use**

Source: US FDA.

<sup>5</sup> In Argentina, Uruguay and other countries, for instance, a patent on a process to produce a tri-hydrate form of docetaxel, an anti-cancer drug, was used to exclude off-patent forms of the drug. A patent on a didanosine tablet for slow release of the active ingredient was used in Argentina to block the commercialization of another, off-patent formulation of the same drug (Levis, 2010).

As suggested by figure 1, the development of new chemical entities for pharmaceutical use presents a worrisome picture. The number of such entities delivered per year has fallen substantially since the 1990s, thereby increasing the average cost of developing new drugs. Furthermore, most new chemical entities do not represent a genuine therapeutic innovation, but present therapeutic effects similar to those of one or more already marketed drugs (*Center for Drug Evaluation and Research*, 2005; Spector, 2005). This decline seems paradoxical for three main reasons. First, since the 1980s and, particularly as the implementation of the Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS Agreement) was completed in developed and developing countries,<sup>6</sup> patent protection allowed companies to increase income generation worldwide through the exercise of stronger and, in some cases, longer patent rights<sup>7</sup> and data exclusivity.<sup>8</sup> Second, there is a new set of scientific and technological tools – such a genomics, proteomics, combinatorial chemistry – that offer the potential of speeding up drug discovery. Mass screening of potential drug candidates has been substituted by more efficient methods enabling the rational design of drugs. Third, the pharmaceutical industry has been one of the most profitable sectors of the economy, fourth only after mining, crude oil production and commercial banking (Commission on Intellectual Property Rights, Innovation and Public Health, 2006). Moreover, funds allocated to R&D have increased since the last decade. The fall in innovative productivity may indicate a crisis in the model of drug development carried out by large pharmaceutical companies, as “the number of new products has not increased whilst the overall level of resources being invested has risen dramatically”

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<sup>6</sup> Transitional periods were provided for developing countries, economies in transition and Least Developed Countries. Developing countries that previously did not recognize pharmaceutical product patent protection could delay its introduction until January 1, 2005 but only a few countries made full use of this term.

<sup>7</sup> The TRIPS Agreement set out a minimum term of 20 years, obliging many countries (including the USA and Canada) to change their legislation.

<sup>8</sup> In the context of free trade agreements (FTAs), as a result of demands made in the process of accession to the WTO, or by the US government or the European Union, several countries have implemented *sui generis* regimes granting exclusivity over the test data necessary to obtain the marketing approval of pharmaceutical products containing new chemical entities. Such exclusivity is not required, however, by the TRIPS Agreement which only mandates protection of test data under the discipline of unfair competition.

(Charles River Associates, 2004). Increasingly, large firms find it more difficult to maintain a continuous pipeline of new and commercially viable products. They heavily depend for new drugs on advances made by small biotechnology companies, while many of the clinical studies are done by specialized contractors and certain segments of biomedical research are undertaken in cooperative ways following an “open access” model, insofar as computational models utilizing genetic information become more important as part of the product development process (Maurer, Rai and Sali, 2004).

Patents over minor incremental developments (often termed as ‘evergreening’ patents<sup>9</sup>) may be used to exclude generic competition and thereby block access to affordable drugs. They may constitute an important obstacle for the realization of the *right to health* recognized in the *International Covenant on Economic, Social and Cultural Rights* and, growingly, in the national constitutions of many countries. The reason for this is that patents obtained (including in relation to drugs already in the public domain) are often strategically used to block generic competition, thereby delaying the entry into the market of medicines at a lower cost. This problem affects developed and developing countries alike. An inquiry by the European Commission, for instance, found that originator companies have designed and implemented strategies (a “tool-box” of instruments) aimed at ensuring continued revenue streams for their medicines. Although there may be other reasons for delays to generic entry, the successful implementation of these strategies may have the effect of delaying or blocking such entry. The strategies observed include filing for up to 1,300 patents EU-wide in relation to a single medicine (so-called “patent clusters”), engaging in disputes with generic companies leading to nearly 700 cases of reported patent litigation, concluding settlement agreements with generic companies which may delay generic entry and intervening in national procedures for the approval of generic medicines. The additional costs caused by delays to generic entry can be very significant for the public health budgets and ultimately the consumer’. The European Commission estimated a loss of around three billion Euros

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<sup>9</sup> ‘Evergreening’ is generally based on the patenting of minor changes to or derivatives of existing products (e.g. formulations, dosage forms, polymorphs, salts, etc.) in order to indirectly extend the life of the original patent over an active ingredient.

due to delays in the entry of generic products caused by misuse of the patent system (European Commission, 2009). The European Commission further found in relation to 219 drugs that:

“...nearly 40,000 patents had been granted or patent applications (as defined above) were still pending...Of the nearly 40,000 cases, some 87 per cent were classified by the companies as involving secondary patents, giving a primary: secondary ratio of approximately 1:7. Of the applications still pending, 93 per cent were classified as secondary (a primary: secondary ratio of approximately 1:13), whilst 84 per cent of the patents granted were classified as secondary (a primary: secondary ratio of approximately 1:5)” (European Commission, 2009).<sup>10</sup>

A critical conclusion from this analysis is that current patent strategies in the pharmaceutical industry may have a direct negative impact on access to drugs, as patents on minor variants/improvements of existing products can be used to block legitimate generic competition, which normally lower prices and make medicines more affordable. In particular, the grant of such patents may, in some cases, force governments that need to ensure access to medicines for its population to grant compulsory licenses, whenever patent owners charge high prices and/or refuse to grant voluntary licenses on reasonable commercial terms. Although compulsory licenses and government use are legitimate under international law, their application has faced considerable resistance from developed countries' governments and retaliations from the pharmaceutical industry. A basic question that arises out in these cases is whether the grant of the patent was justified in the first place and whether governments can avoid the various costs (including of political nature) associated to the grant of compulsory licenses if they applied more rigorous standards in examining the respective patent applications.

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<sup>10</sup> 57 per cent of the 'secondary' patent applications are related to pharmaceutical formulations.

## II PROLIFERATION OF PHARMACEUTICAL PATENTS

The study made in Argentina, Brazil, Colombia, India and South Africa revealed important differences in the size of their economies, their innovation systems and policies and, in particular, in the public health systems and their coverage. However, there is a common need in all these countries to ensure access to medicines to their population, particularly to the segment that lives under the poverty line. As patents allow title-holders to exclude competitors, the proliferation of patents can only mean that prices higher than those that would prevail under competitive conditions will be charged. The larger the number and scope of patents on particular medicines, the greater the likelihood of limitations to access by the poor.

In Argentina, 951 pharmaceutical patents were granted in 2000-2007; in Brazil, 278 patents were granted in 2003-2008; in Colombia 439, in 2004-2008; in India, 2347, in 2005-2008; and in South Africa, 2442 patents were registered in 2008. Although the periods covered in each country are not the same – and the comparability of the data is thereby limited – some interesting conclusions may be drawn from the analysis of these data and the national patent regimes under which patents are issued. It should be noted that while Argentina, Brazil, Colombia and India grant patents based on a prior substantive examination of the applications, in South Africa patents are simply registered without verifying *a priori* if they meet or not the patentability requirements. This explains why South Africa appears with such a comparatively large number of patents issued in one single year.

Based on the average number of patents granted per year, and assuming that pharmaceutical companies are likely to apply for the same patents in all the covered countries, Brazil seems to apply the strictest criteria to assess patentability, followed by Colombia and Argentina. The Brazilian situation may be explained, to some extent, by the mandatory intervention of the health regulatory agency (Health Surveillance Agency – ANVISA) in the assessment of pharmaceutical patent applications,<sup>11</sup> in accordance with article 229(c) of Law 9.279/96.

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<sup>11</sup> ANVISA has applied the patentability criteria in a stricter manner than the Brazilian patent office (Instituto Nacional de Propriedade Industrial – INPI),

India has the largest average number of patents granted per year, but this is possibly a result of the fact that India only started to grant patents on pharmaceutical products in 2005 since, unlike the other countries considered here, it used the transitional period allowed by article 70.8 of the TRIPS Agreement to the full extent, until January 1st 2005.<sup>12</sup> An additional explanation for the case of India is that, as discussed below, the number of patents applied for and obtained by local pharmaceutical companies is quite significant.

Despite the arguments about the positive impact that the introduction or strengthening of patents would have on local innovation in developing countries, the number of patents granted to local companies/individuals in the pharmaceutical field in the studied countries is minimal, with the exception of India. In all the studied countries, pharmaceutical patents overwhelmingly belong to foreign companies, namely from the USA and a few European countries. Figure 2 illustrates the distribution by country of origin of patents granted in Brazil; a similar situation is observable in the other countries (except India).

The results obtained regarding domestic patenting are particularly surprising for Brazil, a country with a large and solid R&D infrastructure. Only one patent out of 287 was identified as owned by a Brazilian manufacturer. In the case of Argentina, only 15 out of 951 patents were obtained by nationals (eight companies, one research institute and 5 individuals) in 2000-2007. In Colombia only two patents in the pharmaceutical field were granted to domestic applicants in the studied period (related to excipients and not to a particular active ingredient). In South Africa, 10 patents were registered by local companies, research institutions or individuals in 2008.

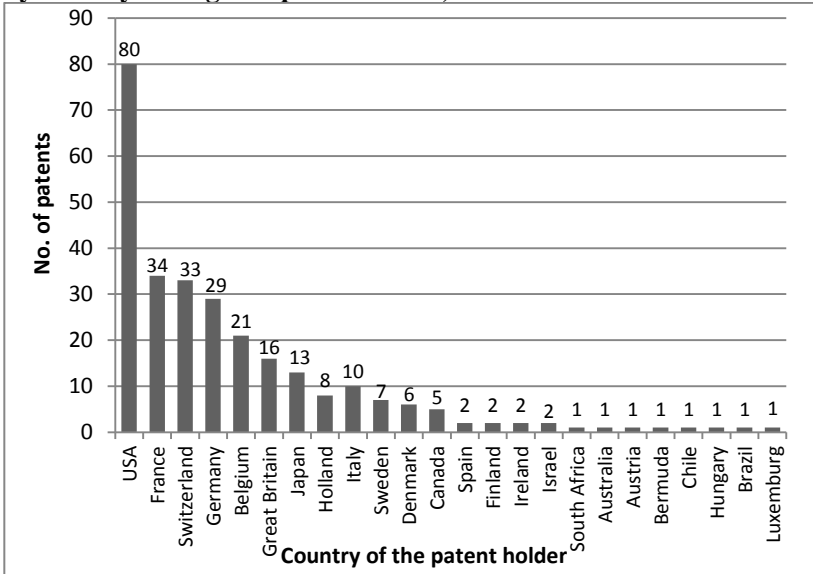
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particularly with regard to second indications and polymorphs. The study, however, found that 6 per cent of the pharmaceutical patents were granted by INPI without being analysed by ANVISA. This raises concerns on whether all pharmaceutical applications are really going through analysis by both bodies.

<sup>12</sup> The mechanism known as 'mail box' established by article 70.8 of the TRIPS Agreement, allowed patent applications to be deposited after 1 January 1995, to be assessed only after the end of the transitional period.



Figure 2

**Brazil: Distribution of patents granted in the pharmaceutical sector by country of origin of patent holder, 2003-2008**

As noted, the situation is radically different in India, which has become a major producer and exporter of active pharmaceutical ingredients and finished medicines. As indicated in table 1 a large portion of the granted patents were filed by local companies.<sup>13</sup> In fact, India itself is apparently the largest source of patents granted in the country. Although R&D for the development of new chemical entities has increased substantially, the large number of grants can only be explained by patents over incremental innovations. The Indian Patent Act was amended in 2005 to introduce, *inter alia*, a special section (section 3(d)) aimed at avoiding ‘evergreening’ patents. This section has not operated, as further elaborated below, as an absolute ban for the patenting of that type of innovations.

<sup>13</sup> However, some of these companies have recently been taken over by foreign pharmaceutical companies.

Table 1

**India: Country of Origin of Patent Owners, 2005-2008**

<b>Country of patent holder</b>	<b>Number of patents</b>
India	588
USA	455
Germany	238
Switzerland	184
Japan	132
United Kingdom	125
France	100
Sweden	74
Netherlands	46
Denmark	42
Belgium	33
Italy	30
Spain	21
Korea, Republic of	20
Israel	16
China	14
Argentina	2
Brazil	2
Cuba	2
Not Available	164

A recent study by the United Nations Development Programme (UNDP) noted in this regard that:

“a number of patent applications relating to a specific polymorphic form of a known compound have been granted, despite the lack of any data provided in the application with respect to enhanced efficacy... More troublingly, however, are those instances where the patent application not only appeared to clearly fall

under one or more of the exclusions contained in Indian patent law, but were also deemed to lack novelty or inventive step in jurisdictions that have much more liberal patentability criteria than India' (Chaudhuri et al., 2010, p. 131)."

The UNDP study found cases of patent applications that were unsuccessful under the 'more lenient patentability criteria' that prevail in the US, which were granted in India, despite the clear legislative intent of preventing evergreening (Chaudhuri et al., 2010, p. 133).

Data on granted patents in the five countries covered in the study also show that the therapeutic use of the patented inventions bear little relation to the profiles of disease prevalent in developing countries. The patented products have overwhelmingly been developed to satisfy the market demand in developed countries. Table 2 shows the classification of the subject matter by therapeutic use for patents issued in the five countries. This table is only illustrative, since in many cases it was not possible to identify the intended use of the claimed invention.

Table 2 suggests that there is little patenting of products or processes for use in relation to diseases that disproportionately affect developing countries. Products for the nervous system, antineoplastic and immunomodulating agents, anti-infectives for systemic use,<sup>14</sup> and products for the alimentary tract and metabolism, concentrate the largest portion of granted patents. The insufficient research and development on the 'diseases of the poor' is a matter of growing concern and one of the main factors that led to the adoption by the World Health Organization of the Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPOA),<sup>15</sup> in the inception of which several of the countries covered by the study played a significant role (Velasquez, 2011).

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<sup>14</sup> This category includes antibacterials for systemic use, antimycotics for systemic use, antimycobacterials, antivirals for systemic use, immune sera and immunoglobulins, and vaccines.

<sup>15</sup> See WHO Resolution WHA62.21.

Table 2

**Therapeutic use of patented products/processes in five countries<sup>16</sup>**

<b>Therapeutic use</b>	<b>No. of patents</b>
A - Alimentary tract and metabolism	589
B - Blood and blood forming organs	146
C - Cardiovascular system	381
D - Dermatology	138
G - Genito-urinary system and sex hormones	168
H - Systemic hormonal preparations, excluding sex	58
J - Anti-infectives for systemic use	707
L - Antineoplastic and immunomodulating agents	785
M - Muscle-skeletal system	233
N - Nervous system	823
P - Antiparasitic products, insecticides and repellents	56
R - Respiratory system	222
S - Sensory organs	58
V - Various	43
L01 - Anti-neoplastic	1

The study of patenting trends in the five countries confirms a significant proliferation of patents on developments of incremental nature and, in many cases, of questionable inventive step. This is well illustrated by the case of India where despite the patentability exclusions provided in section 3 of the Patent Act, a significant number of patents have been granted for possibly non-allowable claims. A total of 688 patents of this kind were identified, including claims on compositions (414) and formulations (137) which only in very exceptional cases would satisfy a rigorous examination of inventive step (Correa, 2006).

Claims covering compositions and formulations are often claims for a new use of a known substance that are not patentable under section 3(d) of the Indian Patent Act. In addition, there is a significant

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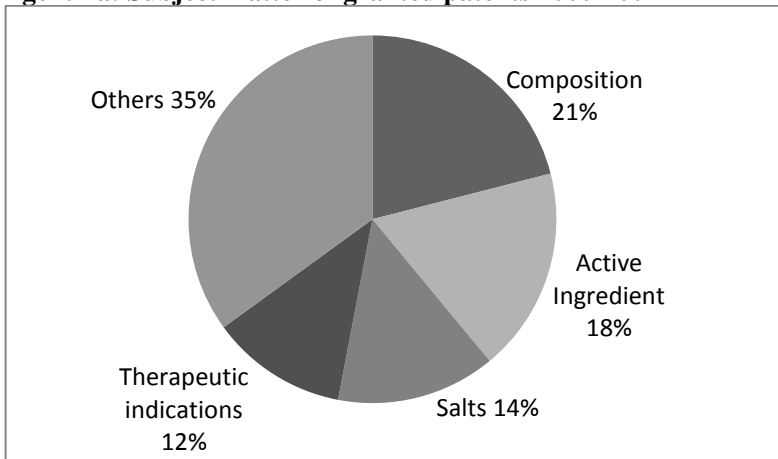
<sup>16</sup> The classification in this table is based on the World Health Organization (WHO) Anatomical Therapeutic Chemical Classification System, available at <http://www.who.int/classifications/atcddd/en/>.

number of patents covering salts, polymorphs and combinations that are also not patentable under section 3(d) as they are considered to be the same substance unless they differ significantly in properties with regard to efficacy. Moreover, a number of ‘method of treatment’ claims that are excluded from patentability under section 3(i) were also granted. This information suggests shortcomings in the way in which section 3 of the Patent Act is being implemented by the patent offices in India.

A similar situation can be found in the other covered countries (where no provision similar to section 3(d) applies). In Argentina, a large number of patents have been granted on salts, compositions, isomers, polymorphs, esters and ethers (Figure 3), including claims on therapeutic indications and doses that are not patentable under Argentine law.

Figure 3

**Argentina: Subject matter of granted patents 2000-2007**



*Source:* Correa et al. (2011) based on information of the Instituto Nacional de Propiedad Industrial.

In Brazil, the study of the patents relating to antiretrovirals (ARVs) showed that a number of them had been granted on ‘compounds’ and formulations (table 3) despite the intervention of ANVISA.

Table 3

**Brazil: Patents Granted on Antiretrovirals, 2003-2008**

Patent number	ARV	Type	Patent holder
PI9506977-1	Key-intermediates for synthesis of protease inhibitor	Chemical	Merck
PI9808060-1	Lamivudine	Formulation	Glaxo Group Limited
PI9815861-9*(WO9961002)	Didanosine	Formulation (enteric coated pharmaceutical composition and method of manufacturing)	Bristol Myers Squibb Co
PI9701877-5	Atazanavir	Compound	Novartis AG
PI9607625-9	Darunavir	Compound	G.D. Searle & Co.

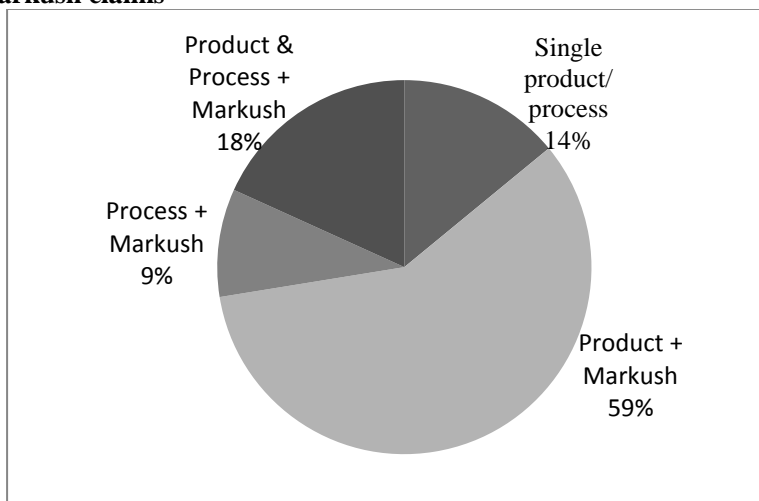
The didanosine case is emblematic, as the active ingredient is in the public domain in Brazil; hence, the government or any other party is free to import or locally produce in Brazil generic versions of, for instance, powder for oral solution. Although the granted patent relates to an enteric coated formulation (Médecins Sans Frontières, 2010), if overbroadly enforced, it may block government's procurement of generic versions of didanosine available in the international market (from companies such as Aurobindo, Cipla and Ranbaxy) or its local production.

In the case of South Africa where, as noted, there is no prior substantive examination of patent applications, it was found that despite the provisions of the Patents Act which set a high standard for patentability, the courts are applying a fairly low standard for patentability. For instance, in a case (Pfizer & Ano v Cipla Medpro & Ors 2005 BIP 1) where revocation proceedings were initiated on the basis that the patent was unclear and obvious the court refused to revoke it, ruling that a besylate salt was unexpected, constituted an advance on the prior art, and represented an inventive step.

Finally, the study found a wide use of the so-called ‘Markush claims’,<sup>17</sup> that is, claims that include a general formula with multiple options that allow for the protection, under a single patent, of up to several millions of molecules. The admission of patents with such claims leads to a rather complex situation when it comes to pharmaceuticals, because a single patent may potentially limit or block research and development on and the commercialization of an extremely large number of products. Figure 4 illustrates the proportion of patents issued in South Africa with Markush claims.

Figure 4

**South Africa: Distribution of patents by type of claim, including Markush claims**



As indicated in figure 4, Markush claims account for the largest portion of all patents issued in South Africa. In the case of Argentina, around 50 per cent of the patents granted in the 2000-2007 period were

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<sup>17</sup> Dr. Eugene A. Markush was the founder and president of Pharma Chemical Corporation of Bayonne, New Jersey. He was a leading manufacturer of dyes in the U.S. Dr. Markush had over 20 patents on synthetic dyes and related fields. In 1924, Dr. Markush obtained a patent on pyrazolone-based dyes (U.S. No. 1,506,316) which protected a generic chemical structure, in addition to the products already synthesized. Since then patenting of such structures were allowed in the USA.

also based on Markush-claims. In India, at least 630 out of the 1432 product patents granted in the examined period contained Markush claims.

Markush claims raise issues concerning sufficiency of disclosure, since normally the patent applicant has empirically obtained only a few of the multiple claimed compounds. In addition, it is virtually impossible to make prior art searches for thousands or millions of compounds. They also pose a transparency problem, since it is very difficult for third parties to identify patent applications that would merit a pre or post-grant opposition. Moreover, in some jurisdictions (including India) after a Markush claim has been granted, it is possible to apply for a patent (usually called ‘selection patent’) on a selection of the molecules originally covered in such a way that protection may be extended for an additional patent term (normally 20 years from the filing date).

It is often argued that patents encourage research and innovation in all fields of technology. This would be achieved through different mechanisms. One of them is through the public disclosure in the patent document of information relating to inventions. However, in conducting the study and developing databases for the five covered countries significant shortcomings were found.

It was amazing, in effect, the number of obstacles and difficulties faced by the research teams to have access to primary and complete information about granted patents. Key words are not reliable enough to determine the status of an individual product or process and the patent coverage. In some cases, there is easy-to-obtain public information on the title of the patent but not on the claims granted or rejected. Moreover, the titles of granted patents are often extremely general, such as ‘pharmaceutical composition’<sup>18</sup>- and the generic name<sup>19</sup> of the active ingredient to which the patent refers is not mentioned in the title, abstract or published claims. In Argentina, for instance, the generic name of the medicine was not mentioned in the information published

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<sup>18</sup> See, e.g., South African patent 2007/01932 (expiry date 05.03.27) held by Bayer Healthcare AG.

<sup>19</sup> ‘Generic’ name is the International Non-Proprietary Name (INN) attributed by WHO to a particular drug.



by the patent office for 80 per cent of the granted patents. This is a particularly serious problem, particularly for those that would be able and willing to file an opposition to the grant of the patent.

In Brazil, the analysis of the specifications and scope of claims is problematic because the documents available on the INPI's website do not contain the claims approved after the examination by INPI and ANVISA. In order to determine the extent to which a particular medicine is protected, it is necessary to request hard copies of the full document to INPI, at the cost of the requesting party and subject to INPI's delivery delays. The same applies in Argentina, where only the title and first claim of the patents are published. In India, the Patent Office has undergone a positive and significant change in the transparency of the information regarding pending and granted patents. The Indian Patent Office has now started publishing granted patents with complete specifications. It is also possible to search patent applications and granted patents through different search variables. However, there remain many shortcomings in the information available as there are several instances in which the ability to obtain full and accurate information is hindered by gaps in information in the Patent Office database.

Resolution 61.21 of the 2008 World Health Assembly, urged the WHO to: "compile, maintain and update a user-friendly global database which contains public information on the administrative status of health-related patents, including supporting the existing efforts for determining the patent status of health products in order to strengthen national capacities for analysis of the information contained in those databases and improve the quality of patents." In the past two years patent information in an electronically search-able format has become increasingly available (Amin, 2010).<sup>20</sup> More and more national patent offices are providing searchable databases, albeit with some providing more information than others. Despite this, it is very difficult to identify patents related to specific medicines in order to establish what 'freedom to operate' exists in a certain field or to make procurement decisions. This is a complex and in many cases unfeasible task, especially for non-specialists, such as procurement agencies in developing countries.

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<sup>20</sup> The Medicines Patent Pool has recently made available a *Patent Status Database for Selected HIV Medicines*. See <http://www.medicinespatentpool.org/patent/search>.

### **III INVENTIVE STEP AND COMPULSORY LICENSES**

A basic argument for the adoption or strengthening of patent protection in developing countries has been that patents may provide the necessary incentives to foster local innovation. As indicated above, this is not clearly the case in four of the five studied countries, where domestic patenting in pharmaceuticals is minimal. In India, as noted, domestic patenting is more significant, but focused on new processes or derivatives/improvements on existing products.

In the case of the pharmaceutical sector, in particular, low patentability standards can have detrimental impacts. A low inventive step is prone to abuses, leading to extension of patent monopolies through products embodying very minor change. There is no basis to assume that such a lower technical requirement would be in favour of developing local production and innovation capacity in developing countries. A lax inventive step allows the grant of patents that extend existing monopolies and guarantee markets for international firms in developing countries, thus making it harder for local firms to overcome constraints.<sup>21</sup> In other words, this would mean that all those variations of the patented product developed by local firms that are very close to the original product will be considered as equivalent to the original and thus an infringement of the patent. More importantly, given the sectoral dynamics of learning, it is unclear how granting patents that fragment and limit the access to underlying processes and products that in the pharmaceutical sector will add value.

As illustrated by the evidence on the studied countries, the application of a low inventive step standard does not promote local innovation, while it favours the deployment of aggressive patenting policies by foreign companies. Even if such low standard would allow local companies to obtain some patents, the costs in terms of limitations to generic competition and, consequently, higher prices for medicines, clearly exceed any benefits that might be generated. From the point of

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<sup>21</sup> In the case of Argentina, for instance, in several cases relating to docetaxel and didanosine, patent owners were able to get provisional measures that immediately excluded competitors from the market, while the competent courts did not find later infringement of the respective patents.

view of an innovation policy in a developing country, it is also questionable whether the patent system should create monopolies for technical developments that do not represent a significant contribution to the state of the art, whether claimed by local or foreign companies, as such monopolies will retard dissemination of innovations that could enhance competition and access to medicines.

A number of developing countries have granted in the last ten years compulsory licenses in the area of pharmaceuticals; there are also a number of cases in which such licenses have been requested but not granted, due to the government's refusal or the adoption of alternative actions or measures, such as price control.<sup>22</sup> Although, as examined in Chapter 7, the majority of compulsory licenses /government use refer to antiretrovirals, products for other diseases have also been covered. Such mechanisms were used either to import or to locally produce the protected drugs, depending on the particular strategies adopted by the governments. In the cases for which information is available, substantial reductions in prices were obtained.

In many of these cases, the need to grant a compulsory license would have not existed, if the patent offices had applied a more rigorous standard of patentability. Thus, lopinavir in combination with ritonavir ('Kaletra') for which a compulsory license was requested in Colombia, is a combination which does not show a new and non-obvious synergistic effect and would not be considered patentable if rigorous standards were used to assess the inventive step. The same would apply to the combination of lamivudine and zidovudine ('Combivir'); a patent on this combination was subject to compulsory license in Malaysia. The patent relating to clopidogrel, subject to a compulsory license in Thailand, relates to a polymorph which, under rigorous patentability standards, would probably not be deemed patentable since polymorphs are not invented but constitute an inherent property of chemical compounds; further, it is obvious for a pharmaceutical manufacturer to find the most suitable polymorph for any particular drug (Correa, 2006).

The extent to which patents subject to compulsory licenses could have been refused through a proper examination of their

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<sup>22</sup> See Chapter 8.

applications would require further and detailed research. The general conclusion that can be made here is, however, that the grant of such licenses is in some cases necessary because the country has not made full use of what is perhaps the most important flexibility under the TRIPS Agreement in the area of patent law: the possibility of rigorously defining the criteria under which the standards of patentability are applied. Article 27.1 of the TRIPS Agreement prescribes, that patents "shall be available for any inventions ... provided that they are new, involve an inventive step and are capable of industrial application", but does not contain any specification about the concept of 'invention' nor about the precise way in which the patentability criteria are to be applied. It has, hence, left World Trade Organization (WTO) Members room to interpret in good faith the concept of 'invention' within their legal systems, and to adopt more or less strict criteria to apply the patentability standards.

In view of the implications of the proliferation of patents with low or inexistent inventive step, governments should adopt rigorous criteria to assess patentability, so as to prevent the granting of patents that do not make a substantive technical contribution to the state of the art (World Bank, 2001) and the use of which may have a negative impact on their development, particularly in the area of public health. In the pharmaceutical sector, in particular, most of patenting is motivated by strategic reasons, namely to restrict generic competition, rather than to protect genuine innovations (the traditional motivation for acquiring patents) (Le Bas, 2007, p. 41).

#### **IV SOME CONCLUSIONS AND RECOMMENDATIONS**

The studies made in Argentina, Brazil, Colombia, India and South Africa have confirmed a diverse but significant proliferation of patents in the pharmaceutical sector that can only be explained by the grant of patents on derivatives/improvements on existing drugs. Many – if not most of them – would not be deemed patentable if more rigorous standards of patentability were applied, in particular in relation to compositions, formulations and polymorphs.

Such studies also revealed little patenting activities in relation to diseases that prevail in developing countries, and an overwhelming concentration of patents in the hands of foreign pharmaceutical companies (with the exception of India). The introduction of product patent protection has made very little in terms of promoting local innovation in pharmaceuticals in those countries.

Although the application of low standards of patentability may allow local companies to obtain patents, the potential benefits for the local industry of such a policy seem to be offset by the costs associated with the proliferation of patents over minor technical changes that may be used to create undue constraints on legitimate competition. Given the asymmetries in innovation capacities between local and foreign industries, low standards of patentability will ultimately benefit the latter. Such standards are unlikely to promote local innovation in pharmaceuticals. Most importantly, the exclusion of legitimate generic competition is likely to negatively affect public health through reduced access to medicines.

Given the flexibilities allowed by the TRIPS Agreement, there is considerable room to define the applicable standards of patentability. In particular, stipulating rigorous criteria to assess inventive step, is an important ex-ante measure that will help prevent abuses by patent holders. The issue of ‘Markush’ claims is also an important aspect that must be analysed in detail, so that the granting of patents with such claims does not become a constraint for research on new compounds or an undue restriction to competition, particularly if ‘selection patents’ are conferred on a narrower group of the compounds covered by the original patent.

Compulsory licenses/government use are important tools that governments can and should use when required to ensure access to affordable medicines. There is a growing number of compulsory licenses granted by developing countries, but generally in the context of political pressures that discourage the further use of that tool. A well-defined policy regarding patentability criteria may avoid, in some – but clearly not in all – cases, the need to resort to such licenses.








Governments should, hence, apply rigorous criteria of inventive step and thereby reduce the scope of speculative or strategic patenting. This would not exclude considering other options to promote local innovation and access to drugs since, obviously, factors other than patenting standards may be relevant to innovation and access to medicines.

In summary, the following policy recommendations can be made for the design of patent policies in developing countries in the area of pharmaceuticals:

- Rigorous criteria to assess the novelty and inventive step of patent applications relating to pharmaceuticals should be applied. Patent offices should develop, in consultation with health authorities, guidelines to examine such applications so as to ensure the patents are only granted where genuine contributions to the state of the art are made.
- Patent claims relating to formulations or compositions, salts, ethers, esters and combinations should be allowed in narrowly defined, exceptional cases. Polymorphs and isomers (when the racemic mixture was already disclosed) should not be patentable.
- Governments should also carefully consider problems relating to sufficiency of disclosure, particularly in the case of the so-called ‘Markush’ claims, so as to ensure that the granting of patents with such claims does not become a constraint for research on new compounds or an undue restriction to competition. ‘Selection patents’ on a narrower group of the compounds covered by the original patent should not be allowed.
- Similarly, claims on second indications of pharmaceutical products, which are equivalent to methods of treatment, should be deemed non-patentable due to lack of novelty and industrial applicability.
- Patent laws should include effective pre-grant and post-grant opposition mechanisms. Governments should encourage civil society’s utilization of such mechanisms through the implementation of simple procedures, timely dissemination of comprehensive information and, where necessary, capacity building.

- In order to improve the transparency of the patent system, the international non-proprietary name (INN) of drugs, when known at the time of filing of a patent application, should be mandatorily disclosed in its title and abstract.
- Compulsory licenses/government use are important tools that governments can and should use when required to ensure access to affordable medicines. The possible invalidation of patents granted should be considered (and legal action taken, where appropriate) before initiating or in parallel to the procedures for obtaining compulsory licenses/government use.
- As patents are unlikely to promote local innovation in pharmaceuticals, governments should consider options other than the patent system to encourage it, particularly with regard to diseases that disproportionately affect the population of developing countries.

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## CHAPTER 2

### HEALTH POLICIES, INTELLECTUAL PROPERTY AND INNOVATION IN ARGENTINA

Carlos M. Correa<sup>1</sup>

#### I. THE HEALTHCARE SYSTEM AND PHARMACEUTICAL POLICY IN ARGENTINA

##### I.1 Registration, Commercialization and Prescription of Pharmaceutical Products

In Argentina all pharmaceutical products require prior registration and authorization for their commercialization and distribution in the country, which is granted by the National Drug, Food and Medical Technology Administration (ANMAT), an agency dependent of the National Ministry of Health.

Law 16.463, Decrees 9763/64, 150/92, amended by Decrees 1890/92 and 177/93 and 1299/97, the Joint Resolutions 988/92 (M.E.y O.y S.P.) and 748/92 (M.S. y A.S.) and the complementary regulations issued by ANMAT, constitute the legal framework that applies to the approval for the sale of medicinal products. The current legislation also requires the previous authorization of manufacturers, importers and distributors of medicinal products.

Law 16.463, enacted in 1964, constitutes the foundation upon which everything related to the manufacturing, production, refining, importation, exportation and storage of pharmaceutical products and procedures is regulated. It also applies to the interprovincial trade of drugs, chemical products, solutions, pharmaceutical formulations, drugs, diagnostic elements and any other product for use in human medicine.

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<sup>1</sup> With the assistance of Paula de Vera.

The law establishes that regulated products “should meet the conditions established in the Argentine Pharmacopeia and if they are not included therein, from the conditions set out by international standards or bibliography of recognized scientific value” (Article 3).

Decree 150/92 and its modifications establish a series of definitions, conditions and procedures for the development of activities pertaining to the registration, manufacture, prescription, refining, distribution, commercialization, exportation and importation of medicines. Decree 177/93 created the Medicinal Products Registry (REM) which makes prior registration mandatory to consider a pharmaceutical product legitimate for sale as provided for under Law 16.463.

These regulations along with Law 24.766 (the “Confidentiality Law”) have instituted the system of “registration via similarity to other pharmaceuticals”, which allows pharmaceutical companies to obtain authorization to commercialize products based on evidence of substantial similarity to another drug which is already registered.

Decree 150/92 (see box 1) established that in the case of products that are already authorized for their commercialization by health agencies from countries with high standards of sanitary surveillance, only the filing of short form documentation would be required in order to obtain sanitary registration in Argentina. This decision aimed at not repeating technical and scientific analyses already carried out under reliable drug oversight agencies. Generic companies can thus rely on the test data developed by “originator” companies. There is no “data exclusivity” in Argentina. In this way, physical and human resources would be rather made available for the tasks of regulation and quality control of medicines. In fact, ANMAT conducts a large number of inspections, whether they are integral inspections for sampling purposes or prior to the launching of products on the market.

However, complete documentation, including pre-clinical and clinical studies, is required by the health authority in cases of new drug or product applications (not registered in Argentina or in any country which has a sanitary surveillance agency with high standards), in order to prove the efficacy and safety of the product for its proposed use.

ANMAT only requires that bioequivalence studies be carried out for medicinal substances that are deemed to be of high health risk as defined in the ANMAT Resolutions 3185/99, 311/01 and complementary resolutions. All antiretroviral drugs are included in this category. Approximately 50 active pharmaceutical ingredients require bioequivalence studies.

Box 1

**Registration of new and ‘similar’ medicines**

***Registration and authorization for the manufacture of drugs***

Complete documentation (product data and pharmaceutical formulation, production method, quality control methods, stability, labels and prospectus and pre-clinical and clinical information) is required in accordance with article 5 of Decree 150/95 in the following cases:

- Novel therapy
- New product (not registered in Argentina or any country with a high standard of health oversight)

Abbreviated information (product data, pharmaceutical formulation, production method, quality control method, stability, data regarding the bioavailability of the product, labels and prospectus) is required as provided for in article 3 of Decree 150/92 when the product is similar to others registered in Argentina or in countries with high standards for sanitary surveillance and pharmacovigilance (countries defined in Annex 1 of Decree No. 150/92).

***Registration and authorization for the commercialization of imported drugs***

Complete documentation is required for registration of products not originating nor commercialized in countries with high standards for sanitary surveillance and pharmacovigilance (Article 5, Decree 150/92).

The requirement of abbreviated documentation applies in the following cases (Article 3 and 4 of Decree 150/92):

- When registration applications are for imports



originating from countries with high standards for sanitary surveillance and pharmacovigilance the following is required: a) evidence of commercialization (packaging, publication in recognized vademecum), b) labels and prospectus, c) quality control methods (for first-time importation only), and d) data regarding the bioavailability of the product;

- When applications refer to imports originating from countries with intermediate standards for sanitary surveillance and pharmacovigilance (countries defined in Annex II of Decree 150/92), which are similar to products already commercialized in Argentina or countries with high level of sanitary surveillance the following information must be provided: a) evidence of commercialization (packaging or publication in recognized vademecum), b) method of manufacture, c) quality control methods, d) stability, e) labels and prospectus, and f) certificate of compliance with Good Manufacturing Practices (GMP) from the production plant, granted by the Argentine health authority, or by the health authority of countries with high standards for sanitary surveillance and pharmacovigilance.<sup>a</sup>

<sup>a</sup> The countries included in Annex I are: the United States, Japan, Sweden, Switzerland, Israel, Canada, Austria, Germany, France, the United Kingdom, the Netherlands, Belgium, Denmark, Spain and Italy. The countries which form part of Annex II are: Australia, Mexico, Brazil, Cuba, Chile, Finland, Hungary, Ireland, The People's Republic of China, Luxembourg, Norway and New Zealand.

In summary, the drug registration system is based on the concept of 'similarity', understood as pharmacological equivalence. Proof of efficacy and safety is only required in the case of new chemical substances, new indications for known chemical substances or new associations not authorized in Argentina or any other country with high standards for sanitary surveillance and pharmacovigilance. In other words, only when it is impossible to demonstrate pharmacological equivalence of the drug being registered based on its prior commercialization in a number of listed countries, does ANMAT require the provision of data regarding efficacy and security obtained in

pre-clinical and clinical studies. This system of registration applies to both domestic and foreign laboratories.

The registration system adopted in Argentina avoids the ethical problems and economic barriers that would arise if second applicants were required to develop and submit their own clinical data, as is the case in countries where ‘data exclusivity’ regimes apply.

## **I.2 Prescription of Medicines by Generic Name**

Law 25.551 on Public Emergency and Reform of the Exchange Regime (2001) declared a social, economic, administrative and financial exchange emergency at the national level. A national health emergency was declared by Decree 486/2001 to guarantee access to health products and services to the Argentine population and, in particular, to:

- Re-establish supply of drugs and supplies to in-patient public institutions;
- Guarantee supply of drugs for ambulatory treatment of patients who are socially vulnerable;
- Guarantee access to essential drugs and the prevention and treatment of infectious diseases;
- Secure access to essential medical services and drugs to the beneficiaries of the social security system.

In this context, upon an initiative of the Ministry of Health, Law 25.649 was approved for the Promotion of the Use of Drugs by their Generic Name in mid-2002. It established that all prescriptions by physicians and dentists must be written using the generic name of the drug, followed by the pharmaceutical formulation, the quantity per package and the concentration.

Argentina does not have specific legislation to regulate the registration, manufacture and commercialization of generic drugs, understood as drugs that have been tested for bioequivalence and bioavailability.

### **I.3 The REMEDIAR Programme**

Before the 2001 economic crisis, the supply of drugs by the national government was carried out through specific programmes for certain pathologies, such as those of low incidence or elevated cost (HIV/AIDS, oncologic diseases, diabetes) and also through hospitals and municipal and provincial health centres for ambulatory treatment.

As a consequence of the economic crisis, in the middle of 2002 the government decided to develop a new drug policy, broader than the previous one, to improve access to essential medicines. The REMEDIAR Programme distributes essential drugs throughout the entire national territory. The central government purchases the required drugs through international tendering procedures to ensure transparency and lower the costs.

### **I.4 Public Expenditure on Healthcare and Medicines in Argentina**

The healthcare system is composed of three sub-sectors: public, private and social security. The last two sub-sectors are closely related, given the high degree of out-sourcing of healthcare services by social security entities to private healthcare providers. The healthcare system is composed of the following institutions:

- a) Public hospitals (national, provincial and municipal);
- b) Union-associated social institutions;
- c) the National Institute of Social Services for Retired and Pensioned (PAMI);
- d) Private health insurance companies.

Healthcare insurers (social welfare and private healthcare insurance) are agents that must finance the costs generated by their beneficiaries. Regarding the financing of drugs, the Compulsory Medical Package (PMO) establishes that insurance companies must bear (co-finance) 40 per cent of the cost of drugs.

Public expense for healthcare included in the General Budget of the Nation for 2010 was 10.16 billion Argentine pesos (equivalent to

USD 2.597 billion) with an increase of 2.3 per cent over the year before. This was equivalent to 6.65 per cent of the Gross Domestic Product (GDP).

Companies with domestic capital control around 50 per cent of the drug market. The total consumption of medicines in Argentina amounted to 587 million units in 2010 with a value of 27.604 billion Argentine pesos, equivalent to USD 7.05 billion in terms of sale prices to the public.<sup>2</sup> Despite this, the Argentine pharmaceutical industry has not achieved the required size and research capacity to develop new chemical substances. Research and development (R&D) has progressed in certain fields such as biotechnology and controlled release of drugs.<sup>3</sup>

The health authorities have launched a “programme for the support of drugs and healthcare products” within ANMAT. This programme, created by Resolution 1719/11 of 15 March 2011, aims at making a specific platform available for the support of R&D projects related to processes and products with innovative characteristics and with an impact on public health.

## **II. MAIN FEATURES OF ARGENTINE PATENT LAW**

Argentina approved the Final Act of the Uruguay Round through Law 24.425, including the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement).

On 30 March 1995, the current Patent Law, Law 24.481 was passed. In September of the same year Law 24.572, the so-called “corrective law”, was enacted to modify several articles of Law 24.481, in response to the veto of several provisions made by the Executive Power under pressure from the US Government. One year later, after a turbulent political process, Decree 260/96 implemented various aspects of the law, as modified.

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<sup>2</sup> Source: IMS Health Argentina.

<sup>3</sup> ISALUD, Serie de Estudios N° 9, *Propiedad intelectual y medicamentos: El caso de la República Argentina*, 2009, pág. 18. ISALUD, Series of Studies No. 9, *Intellectual Property and Drugs: The case of Argentina*, 2009, p. 18.

The adopted patent law has the following characteristics:<sup>4</sup>

- a) Exclusion from patentability of substances already existing in nature, thereby excluding those drugs consisting of proteins or other natural elements,
- b) Adoption of a “principle of international exhaustion of rights” where-under any product legally marketed in another country may be imported without authorization of the patent holder,
- c) The competent authority (for example, the Ministry of Health, or Defence, etc.) may determine exceptions to exclusive rights,
- d) The use of the patent without authorization of the patent holder against payment is possible where:
  - The patent holder refuses to grant a voluntary license under reasonable conditions,
  - The patent is not exploited in the country after three years of its grant or after four years from the date the patent application was filed,
  - The patent holder engages in anti-competitive practices,
  - Public health emergency, national security or any other reason determined by INPI,
  - Dependent patents.
- e) Patents for drugs to be granted from October 2000 onward,
- f) Reversal of the burden of proof applicable to new products in the case of litigation concerning process patents.

In mid-1999 in light of an alleged inconsistency of Argentine legislation with some stipulations of the TRIPS Agreement, the Government of the United States requested consultations with the Argentine Government within the framework established by the WTO for the resolution of disputes.

After several rounds of consultations, the parties arrived at a mutually agreed solution on 31 May 2002, in accordance with which the Argentine Government agreed to send a bill to the National Congress to modify the patent law with regard to: 1) protection of products directly

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<sup>4</sup> ISALUD, p. 59.

obtained with a patented process, 2) provisional injunctions; and 3) reversal of the burden of proof. Consequently, in January 2004, Law 25.859 amended articles 8, 83 and 88 of the patent law to implement the agreement with the USA.

## **II.1 Flexibility in Argentine Law**

### ***II.1.1 Patentable Subject Matter***

Many developed and developing countries have stipulated in their patent laws which objects do not constitute inventions worthy of patent protection, in accordance with the freedom granted by the TRIPS Agreement.

Argentina's legislation addresses what is patentable and what is not as well as certain exclusions including for inventions whose exploitation would not be acceptable for reasons of public order or morality, in order to protect human and animal health or life or the conservation of plants, or in order to avoid serious damage to the environment. Further, in accordance with INPI's Circular No. 008/02 (published on 25 September 2002), the National Administration for Patents shall not grant patents over the second medical use of a known medicine.

A critical aspect for the functioning of the pharmaceutical market is related to the standards of patentability applied to award patents. Lax standards lead to the proliferation of patents with little or no inventive step that can be used to prevent or delay the entry of generic products to the market.

### ***II.1.2 Compulsory Licensing***

Compulsory licenses can be granted by the National Institute for Intellectual Property according to the circumstances of each case. The reasons enumerated in the patent law for the grant of a compulsory license are: refusal to deal (Article 42), lack of exploitation (Article 46), anti-competitive practices (Article 44), health emergency or national security (Article 45), dependent claims (Article 46) and non-commercial

use (Article 47). To date, Argentina has not granted any compulsory licenses.

### **II.1.3 Experimental Use and the “Bolar” Exception**

Exceptions for experimental use are allowed by the majority of countries with some differences as to the scope. The Argentine patent law establishes in Article 36 that patents shall have no effect against a third party who in a private or academic environment and with no commercial intent, carries out research activities of an experimental nature, and for this reason uses or manufactures a patented product or process.

The law seems to limit the scope of this exception by determining that the use of an invention should refer to activities that are exclusively academic or experimental without commercial objectives.<sup>5</sup> However, experiments can be carried out with many different objectives, for example, in order to prove the executability of a patented invention, determine the validity of the claims, establish unknown effects or new uses of the patented invention, or study the possibilities to improve on it.<sup>6</sup> The law is not clear regarding the scope of the exception since it would not be possible, in every case, to determine with certainty whether the intention of carrying out a test or using a patented invention is commercial or not.

Despite the fact that the patent law seems to limit this exception to non-profit research activities, later the Confidentiality Law 24.766 introduced, in Article 8<sup>7</sup> an exception for experimental use with commercial objectives.<sup>8</sup> This exception specifically allows experimentation carried out with the objective of submitting an

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<sup>5</sup> Correa, C., “Propiedad Intelectual y Salud Pública”, *La Ley*, 2006, pp. 137-138.

<sup>6</sup> See, for example, SCP/13/3, WIPO, Exclusions from Patentable Subject Matter and Exceptions and Limitations to the Rights, p. 30.

<sup>7</sup> Art. 8 - When a product or process is protected by a patent any third party can use the invention before the patent expires with experimental purposes and in order to gather the information required for the approval of the product or process by the corresponding authority in order for its commercialization after the patent expires.

<sup>8</sup> Correa, C., “*Derechos de Propiedad Intelectual, Competencia y Protección del Interés Público*”, Editorial BdeF, Montevideo-Buenos Aires, 2009, p.224.

application for approval of commercialization of a pharmaceutical product during the lifetime of a patent (“Bolar exception”).

#### ***II.1.4 Parallel Imports***

The patent law establishes in Article 36, inc. c) the principle of international exhaustion of rights. Rights conferred by the patent cannot be exercised “against anyone who acquires, uses, imports or commercializes the product in any manner”. Any importation into the country will be considered legal when there is consent by the patent holder or where the product has been commercialized in the exporting country by a compulsory licensee.<sup>9</sup>

The regulatory decree 260/96 seems to reduce the scope of the exception to two situations: a) when the authorized licensee for marketing in the country proves that it is authorized by the patent holder in the country of procurement, or b) proves that it has been authorized to do so by a third party authorized to commercialize the product.

This topic was the subject of consultation between Argentina and the United States under the dispute settlement mechanism of the WTO. After some discussion, the agreed understanding was based on a reading of the law provision in conjunction with the regulatory decree. However, who may be an “authorized third party” to commercialize the product was not determined. Thus an authorized third party could be a person acting under a compulsory license or one who markets the patented product in a market where it is not protected. Therefore, the extent of exhaustion in the Argentine legal system is still open to debate.

#### ***II.1.5 Protection of Undisclosed Information***

Law No. 24,766, known as the "Confidentiality Act" was enacted in order to incorporate the protection required by the TRIPS Agreement in Section 7 with respect to undisclosed information. Chapter II of the law specifically refers to the protection of information requested by the health authority as a condition for the approval of pharmaceuticals. Article 4 provides that in cases where registration is requested for

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<sup>9</sup> Correa, C., “Derecho de Patentes”, *Ediciones Ciudad Argentina*, 1996, p. 149.



products that employ new chemical substances which have no prior registration in Argentina or in any other country with high standards for health regulation, all information necessary to demonstrate the efficacy and safety of the products must be submitted. Article 5 contains the requirements that must be met to approve products that are already registered by the national health authority or in any of the countries with high standards of health regulation. Lastly, Chapter III identifies the actions to be taken in case of violation of the law. The protection conferred under this law does not create exclusive rights for anyone who controls or has developed the information (Article 11).

The law stipulates the exact nature of the information that must be submitted to obtain marketing authorization for products that are already registered. It further provides that approval of the registration of “similar” products by the local authority does not imply the use of confidential information protected by this law. This has been confirmed by the federal courts in a ruling of Chamber III of the Federal Court of Appeals on Civil and Commercial Matters in the case *Novartis v. Monteverde*.<sup>10</sup> Among other considerations, the court stated that the approval of “*like products*” under Law 24,766 and other regulations (Decree 150/92) does not, by itself, imply breach of the obligation that Argentina assumed to prevent “*unfair commercial use*” of “undisclosed information” (Art. 39.3 TRIPS), nor does it mean “*unfair commercial use*” (Art. 39.2 TRIPS).

The court also held that the TRIPS Agreement leaves the decision of how to regulate this issue to each WTO Member in one of two ways: one is under the discipline of unfair competition, a situation that does not prevent the approval by health authorities of third parties’ applications for generic medicines, based on similarity; the other grants exclusive rights to undisclosed data for a certain period. Economic and technological inequalities and the needs of each Member justify the decisions taken. Needless to say, the adoption of the second option could only be carried out by issuing regulations that expressly provide the terms of this higher protection; since an express provision

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<sup>10</sup> Causa N° 5.619/05 “*Novartis Pharma AG c/ Monte Verde SA s/ Varios Propiedad Industrial e Intelectual*”, (Sentencia del 01/02/2011), Sala III. *Novartis Pharma AG vs. Monteverde SA, Intellectual and Industrial Property, Judgment Feb. 01, 2011, Courtroom III.*

establishing a higher standard of protection for such data does not exist in Argentina.

It is noteworthy that one of the topics included in the consultations initiated by the US Government with the Argentine Government under the WTO dispute settlement mechanism was the interpretation of Article 39.3 of the TRIPS Agreement. Both governments agreed that the differences in interpretation would be resolved through the Dispute Settlement Understanding of the WTO. In this regard it was agreed that the US could decide to continue the consultations or request the establishment of a panel in relation to that article. It was also agreed that in case the Argentine legislation were inconsistent with any DSB ruling clarifying the content of the rights related to the protection of undisclosed test data submitted for marketing approval in accordance with paragraph 3 of Article 39.3 of the TRIPS Agreement, Argentina would submit an amendment of the legislation to the National Congress, within one year in order to comply with Article 39.3.

After nine years no complaint has been made against other WTO Members that do not grant “data exclusivity”. This strongly suggests that the Argentine and similar legislations are fully consistent with the TRIPS Agreement.

### ***II.1.6 Pre-grant Filing of Observations from Third Parties***

Argentina's legislation provides for the possibility of submitting observations before the granting of a patent. Article 28 of the patent law provides that any third party may make observations on the patent application and submit supporting documentation, within sixty days of publication of the application. These observations should refer to the legal requirements for the granting of the patent. After expiry of that period, INPI admits the submission of observations, but examiners are not bound to consider them. In any case, the person submitting observations does not become a party to the procedure.

### ***II.1.7 Preliminary Injunctions***

The patent law introduced provisions on preliminary injunctions in case of alleged infringement of patents, incorporating the so-called "incident

of exploitation", under which the alleged infringer could continue to use the invention against the deposit of a guarantee.

In January 2004, Law 25,859 amended Articles 83 and 87 of Law 24,481 according to the text contained in the agreement reached with the United States following the claim made in the WTO. The new wording of Article 83 lays down specific conditions for the granting of such injunctions.

The first decisions on preliminary injunctions under Law 24,841 took into account the system laid down in Article 87, and then set aside this specific system in order to implement one structured around Articles 230 and 232 of the CPCC Code, and Article 50 of TRIPS. Almost all the requested preliminary injunctions were granted "inaudita parte".

Following the reform of Argentine legislation on patents in 1995, litigation in the pharmaceutical market increased significantly. This type of litigation was rare before the new patent law entered into force. The granting of patents for derivatives or variants of existing products has been one of the reasons for that increase, associated with the ease with which patent holders could obtain injunctive relief *inaudita parte* with immediate exclusion of a potential infringer from the market.

After the amendment to Article 83, the judges continued for some time to directly apply Article 50 of TRIPS and Article 232 of the CPCC. It took some time before the courts finally applied the new requirements set out by the amended article 83, including the need for a prior expert opinion. As a result, there has been a reduction in both applications for and granting of these measures.

### **III. OVERVIEW OF PHARMACEUTICAL PATENTS GRANTED IN ARGENTINA <sup>11</sup>**

#### **III.1 The New Scenario**

A total of 951 pharmaceutical patents were granted in Argentina, in the period 2001-2007. These patents have been granted under two different legal frameworks, Law 111 of 1864 and Law 24.481 (as amended) of 1995. Although 24.481 *Law on Patents and Utility Models* was enacted in 1995, the protection of pharmaceutical products only came into force in October 2000, as a result of the (partial) application of the grace period granted to developing countries by Article 65 of the TRIPS Agreement. Until then, only the protection of manufacturing processes of pharmaceuticals existed in Argentina, based on Law 111 of 1864.

The following analysis is limited to granted patents. The dates of application considered below do not refer to all applications submitted to INPI, but only to those that were finally granted. Therefore, neither those applications that were rejected by INPI nor those that were not yet granted by 2007 were considered. The same applies to the analysis of expiration dates.

The greatest number of applications is concentrated from 1995 through 1998, representing 64 per cent of the total number of applications received during the period of the study. After 1998, the quantity of applications has decreased year after year until arriving at the unit figure in 2004 and 2005.

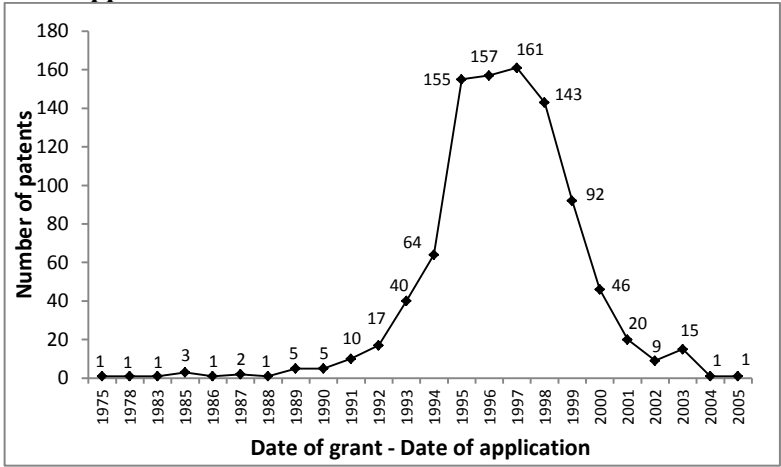
Figure 1 shows the evolution of pharmaceutical patents granted until 2007 according to the date the application was registered by INPI. It clearly shows the impact of the implementation of the TRIPS Agreement with regard to pharmaceuticals.

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<sup>11</sup> Comisión Nacional Salud Investiga. This section is substantially based on Carlos Correa, Cynthia Balleri, Marina Giulietti, Federico Lavopa, Carola Musetti, Gastón Palopoli, Tomás Pippo, Catalina de la Puente, Vanesa Lowenstein, *Patentes, suministro de medicamentos y protección de la salud pública*, *Revista Argentina de Salud Pública*, 2011; 2(7):19-27.

Figure 1

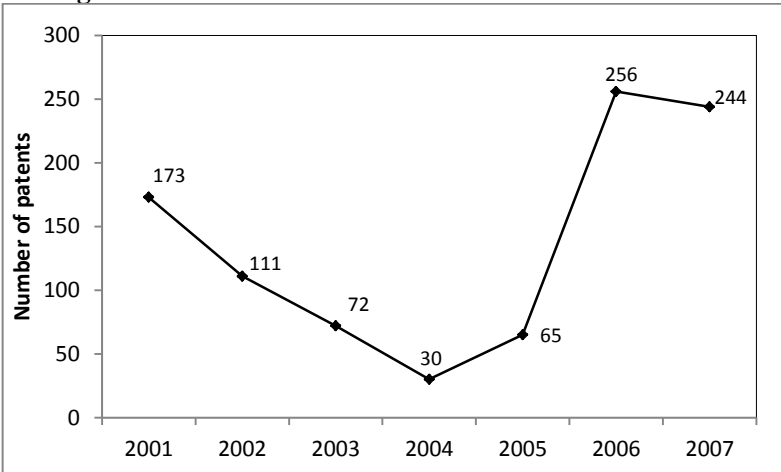
**Trend of pharmaceutical patents granted until 2007 according to year of application**



Source: Based on information published by INPI.

Figure 2

**Trend of pharmaceutical patents granted until 2007 according to year of grant**

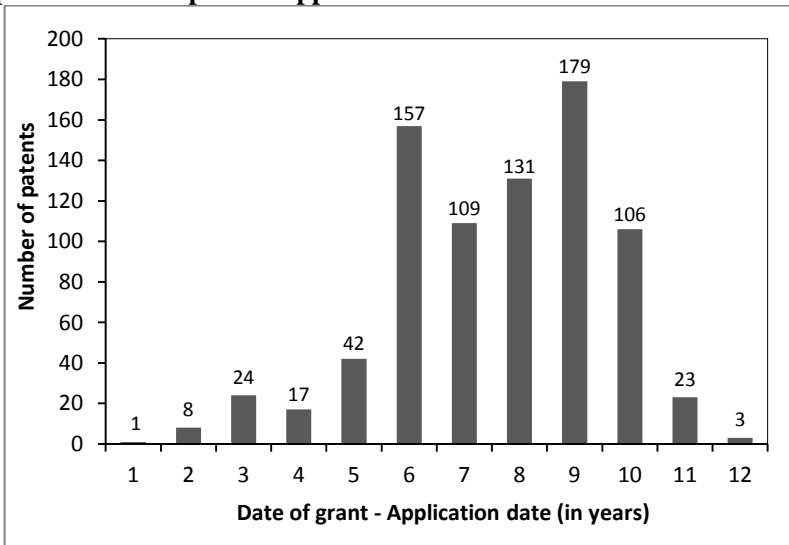


Source: Based on information published by INPI.

The grant of pharmaceutical patents is subject to large fluctuations. Figure 2 shows two years in which the number of patents granted increased substantially: 2001 and 2006 with 173 and 256 patents granted respectively. Nevertheless, between these two years there was a period of sustained decline until reaching as low as 30 grants in 2004.

Figure 3 shows the time gap that exists between the date of application and the granting of applications between 1995 and 2007. This analysis comprises 800 patents. On average the lapse between the date of application and granting was 7.6 years, while the extreme values were 1 to 12 years. The time gap mode, the gap that was most frequent, was nine years, comprising of 179 patents.

Figure 3  
**Time gap between the date of application and granting of pharmaceutical patents applied for from 1995 onward**



Source: Based on information published by INPI.

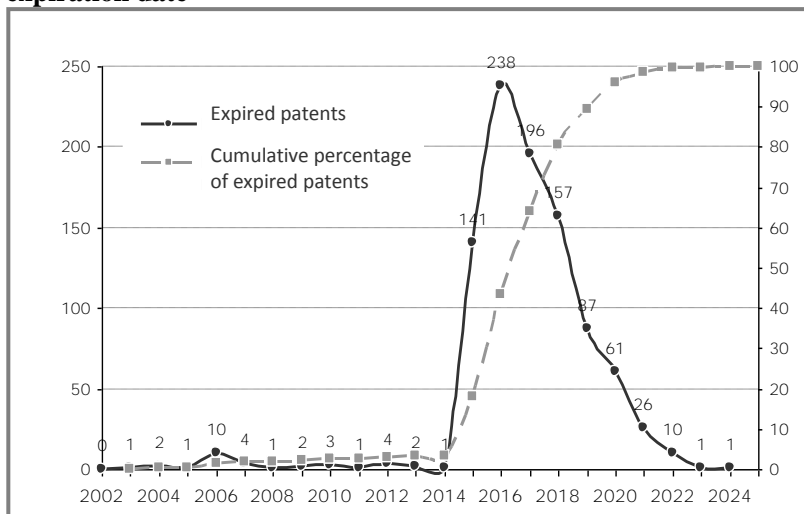
The case in which the time gap between application and granting was one year was a process patent which corresponds to Eli Lilly; the application was presented in 2005 and granted in 2006.

In Argentina, and according to the stipulations in Patent Law 24.481, the duration of patents is 20 years from the date of application. Figure 4 shows that the largest number of patents will expire in 2016, with 238 patents expiring in that year, representing 25 per cent of the total number of patents.

Around 2016 there will be the largest number of expiring patents given that in 2015 there will be 141 patents expiring, while in 2017 and 2018, 196 and 157 patents will expire respectively. As a result, by 2018, 80 per cent of all patents granted until 2007 will have expired.

Figure 4

**Trend of pharmaceutical patents granted until 2007 according to expiration date**



Source: Based on information published by INPI.

Table 1 presents the classification of patents granted until 2007 according to the nationality of the patent holders. 951 patents granted have been classified in the following categories: Argentina, United States, Switzerland, European Union and others. The greatest participation corresponds to patent owners based within the European Union, with a total of 410 patents, representing 43 per cent of the total number of patents granted. In second place and with a participation of 36 per cent, are patents from the United States whereas the number of

domestic patents is 15 or 2 per cent of the total number of patents granted.

Table 1

**Relative participation, according to the nationality of the patent holder of pharmaceutical patents granted until 2007**

<b>Nationality of pharmaceutical patent holder</b>	<b>Number of patents</b>	<b>Percentage</b>
European Union	410	43%
United States	340	36%
Others	96	10%
Switzerland	90	9%
Argentina	15	2%
<b>Total</b>	<b>951</b>	<b>100%</b>

*Source:* Based on information published by INPI.

The leadership of the European Union is not recent. Figure 5 shows the trend of the relative participation of nationalities through the years. It shows that the relative participation of European block countries has been above 40 per cent with the exception of 2002 and 2005. Meanwhile, companies based in the United States topped this ranking in 2002 and 2005 with 42 per cent and 51 per cent respectively. The greatest annual participation of patents granted to domestic applicants was in 2003 with 4 per cent. In 2007 the greatest number of patents was granted; 7 patents compared to 3 in 2003.

Companies with domestic capital control around 50 per cent of the drug market. Despite this, the Argentine pharmaceutical industry has not achieved the required size and research capacity to develop new chemical substances Research and development (R&D) has progressed in certain fields such as biotechnology and controlled release of drugs.<sup>12</sup>

The health authorities have launched a “programme for the support of drugs and healthcare products” within ANMAT. This

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<sup>12</sup> ISALUD, Serie de Estudios N° 9, *Propiedad intelectual y medicamentos: El caso de la República Argentina*, 2009, pág. 18. ISALUD, Series of Studies No. 9, *Intellectual Property and Drugs: The case of Argentina*, 2009, p. 18.



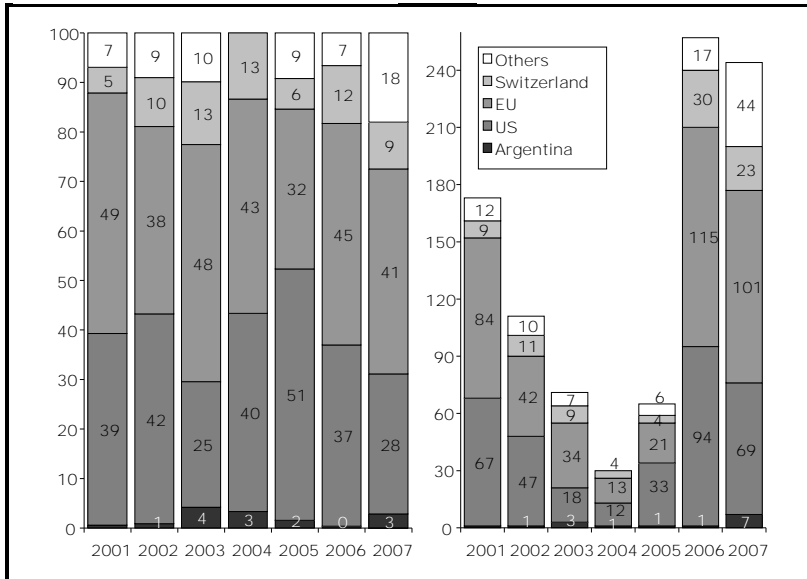
programme, created by Resolution 1719/11 of 15 March 2011, aims at making a specific platform available for the support of R&D projects related to processes and products with innovative characteristics and with an impact on public health.

Figure 5

**Participation of nationalities of pharmaceutical patent holders**

Percentage of patents granted according to nationality of patent holder per year.

Number of patents granted according to nationality per year.



Source: Based on information published by INPI.

In total, 235 pharmaceutical companies<sup>13</sup> have been identified as the owners of the 951 patents granted. Note that the greatest

<sup>13</sup> In order to put together the list of pharmaceutical companies, the following methodology was used: Patent holders who could easily be related, were put together in a single group. For example, Abbott GMBH & Co. KG and Abbott Laboratories were considered under the same Abbott Group. The rest of the patent holders were considered as single laboratories.

concentration of these patents, 50 per cent correspond to 14 companies while 60 per cent are held by 21 companies.

In the following table the top 20 laboratories in terms of number of patents granted are presented. F Hoffman-La Roche AG, of Swiss capital, occupies the top of the list of patents granted with 64 patents, representing 7 per cent of the total. In second place was the Pfizer Group with 61 patents, followed by the Merck Group with 50 patents.

Table 2

**Number and percentage of patents granted to the top 20 patent owners**

<b>Laboratory</b>	<b>Pharmaceutical patents granted per laboratory</b>	<b>Percentage of total patents granted</b>	<b>Accumulated percentage</b>
F Hoffmann-La Roche AG	64	7	7
Pfizer Group	61	6	13
Merck Group	50	5	18
Astra Group	47	5	23
Eli Lilly and Company	42	4	28
Sanofi Group	39	4	32
Janssen Group	32	3	35
Bayer Group	29	3	38
Glaxo Group	26	3	41
Novartis Group	24	3	44
Aventis Group	19	2	46
Wyeth Group	18	2	47
Schering Group	17	2	49
SmithKline Group	17	2	51
Hoechst Aktiengesellschaft	15	2	53
Syntex Group	14	1	54
Bristol-Myers Squibb Company Group	13	1	55

<b>Laboratory</b>	<b>Pharmaceutical patents granted per laboratory</b>	<b>Percentage of total patents granted</b>	<b>Accumulated percentage</b>
Abott Group	12	1	57
Hoechst Marion Rousssel	12	1	58
Société de Conseils de Recherches Group	12	1	59
<b>Total of 20 laboratories</b>	<b>563</b>	<b>59</b>	
<b>Total number of patents granted</b>	<b>951</b>	<b>100</b>	

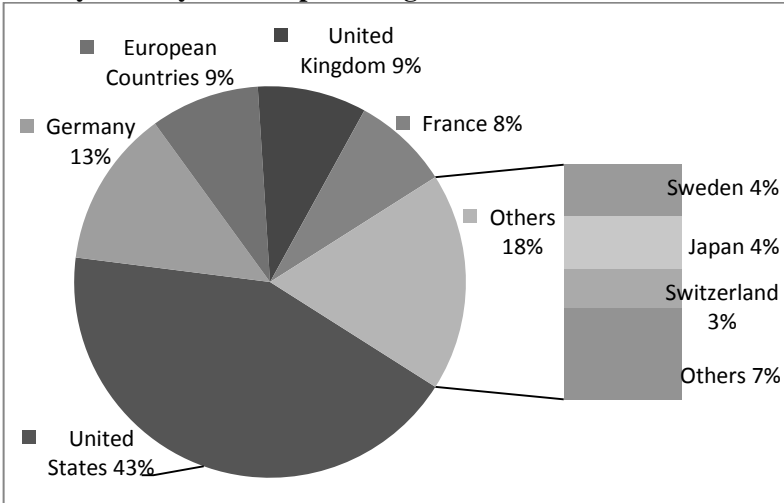
*Source:* Based on information published by INPI.

Finally, the last aspect analysed in this section concerns the country priority code which refers to the country where the first application has been filed.

Regarding the 951 pharmaceutical patents granted, in 68 cases the country priority code was not identified in the published information. This could be the result of an omission of information, meaning that the priority had been applied for but the data was not entered into the electronic database of INPI, there was no previous application, or it was the decision of the applicant not to invoke priority under the Paris Convention. In the following analysis, it was decided to methodically exclude the 68 patents whose priority was not indicated.

Table 3 shows the quantity and percentage of pharmaceutical patents granted according to Country Priority Code, where we observe that patents applied for previously in the United States and Germany made up more than half of the priorities (56 per cent).

Figure 6  
**Country Priority Code in percentage**



Source: Based on information published by INPI.

Table 3  
**Quantity and percentage of patents granted up until 2007 according to Country Priority Code**

Country code	Country	Frequency	Percentage
US	United States	382	43
DE	Germany	111	13
EP	European Office	76	9
GB	United Kingdom	76	9
FR	France	73	8
Others		165	18
	Total	883	100
No priority indicated		68	

Source: Based on information published by INPI.

### III.2 Characteristics of Pharmaceutical Patents

The majority of patents claim therapeutic uses targeted at the Nervous System, with 114 patents, and Anti-infectious Agents of Systemic Use (except antiretrovirals) with 101 patents, representing 12 per cent and 11 per cent of the total, respectively.

In the case of 221 patents, it was not possible to determine the therapeutic use. These are indicated in the following table as “undetermined” and represent 23 per cent of the granted patents.

Table 4 presents a list of the total number of pharmaceutical patents granted grouped according to therapeutic use.

Table 4

#### Number and percentage of patents granted until 2007 according to therapeutic use

Therapeutic use	Frequency	Percentage
Nervous System	114	12
Anti-infectious agents for Systemic Use (except antiretrovirals)	101	11
Gastrointestinal tract and metabolism	77	8
Oncologic	71	7
Cardiovascular system	56	6
Anti-neoplastics and Immunomodulators (except oncologics)	45	5
Systemic hormonal preparations, sexual hormones and insulins	42	4
Muscular-Skeletal System	39	4
Respiratory System	32	3
Blood and Hematopoietic organs	31	3
Anti-parasitic, Insecticides and Repellents	26	3
Antiretroviral	20	2
Genitourinary System	15	2

<b>Therapeutic use</b>	<b>Frequency</b>	<b>Percentage</b>
Dermatologic	13	1
Sensory Organs	9	1
Various	7	1
Others	32	3
Undetermined	221	23
<b>Total</b>	<b>951</b>	<b>100</b>

Source: Based on information published by INPI.

Additionally, 111 of the 951 patents granted have been identified with “Other Therapeutic Uses” as a complement to the principal use (representing 12 per cent of the total).

There may also be claims on procedures of manufacturing as well as claims regarding the use of the product (though the latter are not admissible under Argentine law). Claims can be presented individually (that is, Product) or as a combination (Product and Process), though the second case would be referred to in this study as “multiple” claims. The “Markush” type claims refer to a chemical structure that possess multiple allowed chemical substitutes, supposedly functionally equivalent, in one or more parts of the compound. This means that they can include millions of possible compounds.

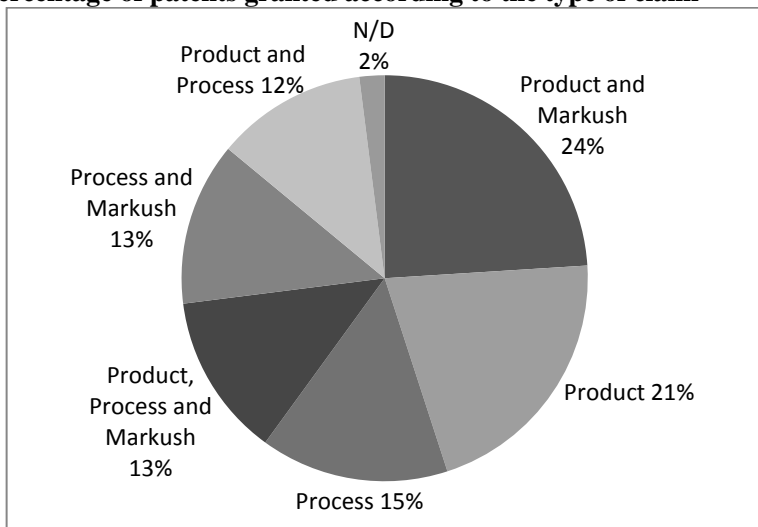
Figure 7 shows the percentage of patents granted according to type of claim. These have been grouped into the following categories:

1. Product
2. Process
3. Product and Process
4. Product and Markush
5. Process and Markush
6. Product, process and Markush

The Product and Markush type of claims account for 24 per cent of the total (227 patents). In second place are the claims of the product type with 199 patents.

Figure 7

**Percentage of patents granted according to the type of claim**



*Source:* Based on information published by INPI.

The database contains 592 patents with claims of the multiple type, corresponding to 134 patentees. Therefore these patents represent 62 per cent of patents granted.

Table 5 shows the 20 companies with the highest number of patents with multiple claims. In the first place is F. Hoffman-La Roche AG with 55 patents. Taking into account that this company holds a total of 64 pharmaceutical patents granted by INPI, multiple claims represent 86 per cent of its portfolio.

A large number of pharmaceutical patents were found to cover variants or derivatives of known active ingredients. To be exact, 181 claims on salts were identified, 41 on isomers, 14 on polymorphs, 13 on esters and 4 on ethers.

Table 5

**Companies with the largest number of multiple claims**

<b>Companies</b>	<b>Pharmaceutical patents granted per laboratory</b>	<b>Patents with multiple claims</b>	<b>Percentage of patents with multiple claims/total number of patents</b>
F Hoffmann-La Roche AG	64	55	86
Pfizer group	61	43	70
Merck group	50	32	64
Astra group	47	29	62
Sanofi group	39	29	74
Janssen group	32	27	84
Eli Lilly and Company	42	20	48
Glaxo group	26	18	69
Novartis group	24	17	71
Aventis group	19	15	79
Bayer group	29	14	48
Hoechst Aktiengesellschaft	15	12	80
SmithKline group	17	11	65
Hoechst Marion Roussel, INC	12	11	92
Syntex group	14	10	71
Abott group	12	9	75
Wyeth group	18	9	50
Florida State University	10	8	80
Schering group	17	8	47
Société de Conseils de Recherches Group	12	8	67

*Source:* Based on information published by INPI.



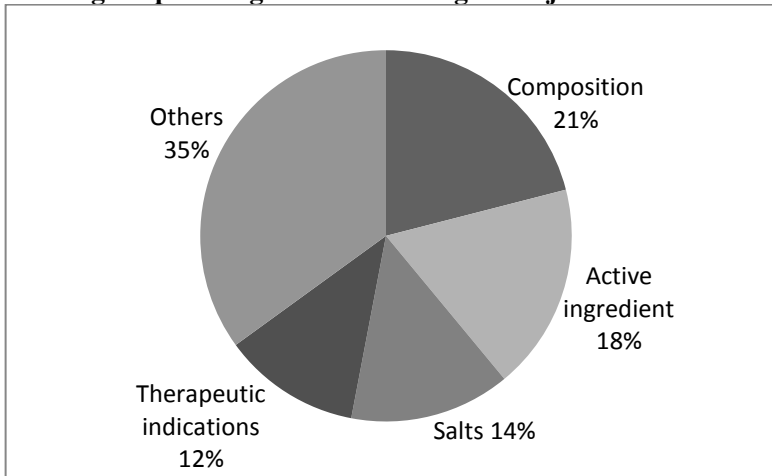
This indicates that lax patentability criteria are applied, which promotes the practice of “evergreening” that artificially extends the term of protection through small modifications to the originally patented product.

Claims were also found that are not patentable according to Argentine legislation. For example, 156 patents were found that claim therapeutic use and 72 claims on dosages. A more thorough study would be necessary in order to establish exactly what subject matter is being protected in these cases.

To summarize, a total of 1319 claims were counted (noting that one patent may contain more than one claim) with a majority of composition claims (21 per cent), followed by those on active ingredients (18 per cent), salts (14 per cent) and therapeutic indications (12 per cent). “Others” include claims on polymorphs, isomers, mixtures of isomers, complexes, combinations, formulation, dosage, esters, ethers, metabolites, pure forms, and other derivatives and intermediates.

Figure 8

**Percentage of patents granted according to subject matter claimed**



Source: Based on information published by INPI.

Finally the quality of the information found on the website of INPI accompanying the publication of each patent was analysed in order

to assess the accessibility of information on substances protected under each granted patent. The analysis suggests that out of 951 pharmaceutical patents granted, 78 per cent did not indicate the generic name of the products. This meant that pharmaceutical specialists have had to work hard to establish the respective generic name.

In the case of 32 patents, the information presented was insufficient or confusing. This situation is reflected as “undetermined” in table 6.

Additional studies will be necessary in order to establish if the covered products have a generic name and what the names are.

To summarize, 771 patents were found for which generic names were not easily inferred. Even if the current legislation does not contemplate an obligation to disclose the generic names or INN, the implementation of this requirement is highly recommendable in order to make the patent application and granting process more transparent and efficient. This requirement is easily incorporable in all patent applications, with the exception of those related to new chemical substances.

Table 6

**Indication of generic name in published information**

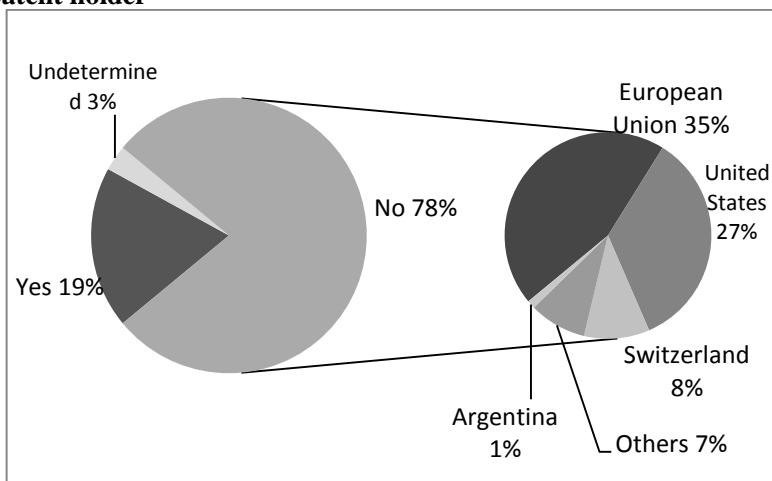
<b>Indicates generic name</b>	<b>Number</b>	<b>Percentage</b>
Yes	180	19
No	739	78
Undetermined	32	3
<b>Total</b>	<b>951</b>	<b>100</b>

*Source:* Based on information published by INPI.

When the national origin of the 739 patents that do not indicate a generic name is examined, it is observed that the European Union holds the majority of these with 327 patents (44 per cent), and the United States follows in second place (34 per cent).

Figure 9

**Lack of indication of generic name, according to the nationality of patent holder**



Source: Based on information published by INPI.

**III.3 Profile of Pharmaceutical Patenting by Domestic Companies**

The United States whose market “accounts for 30 per cent of world sales, Japan, France and Germany...is the vanguard of new technological discoveries and have carried out the larger part of the research and development of new products”.<sup>14</sup> For this reason it comes as no surprise that these are the countries at the top of the ranking of patents granted.

Nevertheless, some domestic laboratories and other entities or individuals in Argentina filed applications out of which 15 patents were granted in the considered period.

<sup>14</sup> González García G., de la Puente C., Tarragona S.: *Medicamentos: Salud, Política y Economía*. Buenos Aires, Ediciones ISALUD, 2006, pag. 84. Medicine: Health, Politics and Economy.

The following table presents the list of domestic companies, institutions and individuals that hold at least one pharmaceutical patent granted by INPI. The list is composed of 14 patent owners and 15 patents. One laboratory, GADOR S.A., holds two patents while the rest have one patent each.

Table 7

**Pharmaceutical patents of domestic origin**

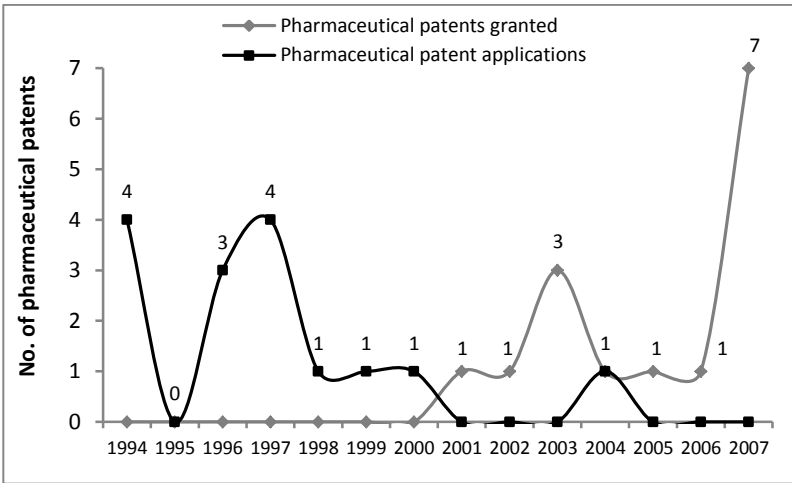
<b>Patent holder</b>	<b>Pharmaceutical patents granted</b>
BALDESSARI, ALICIA	1
BIO SIDUS S.A.	1
BIOFARMA S.A.	1
BIOGENESIS S.A.	1
BIOVACS INC	1
BLANCO, GUILLERMO JAVIER, GIL	1
DECOFARMA S.A.	1
GADOR S.A.	2
INST. INV. de las FFAA	1
IRAZOQUI, FERNANDO JOSE	1
JOISON AGUSTIN NESTOR	1
OSMOTICA ARGENTINA S.A.	1
OUTOMURO, PABLO	1
SYNTEX S.A.	1
<b>Total</b>	<b>15</b>

*Source:* Based on information published by INPI.

Figure 10 permits the visualization of the trend of patents granted to domestic laboratories until 2007 according to the date of application and grant. With respect to the year of grant, the data shows a stable tendency with the exception of two years where there were two peaks 2003 (with 3 patents) and 2007 (with 7 patents), while in other years only one patent was granted. Regarding the date of application, there has been a stable trend since 1998 although the concentration of peaks fall around the period 1994-1998, when more than 70 per cent of the domestic patent applications were filed.

Figure 10

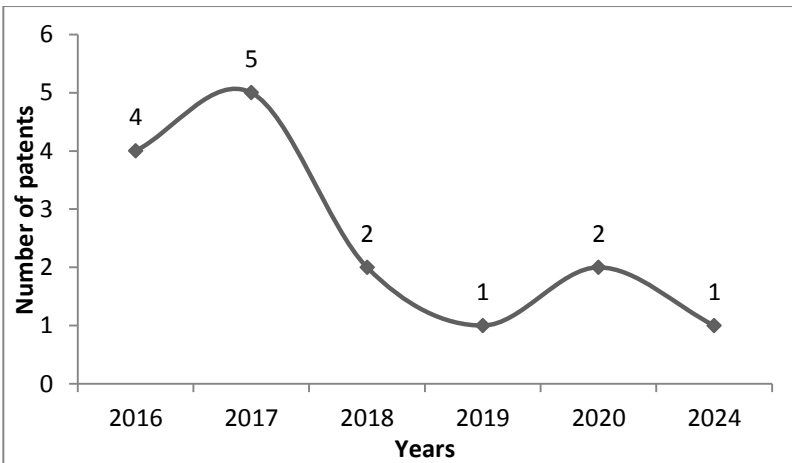
**Evolution of pharmaceutical patents granted to domestic applicants according to year of application and granting**



Source: Based on information published by INPI.

Figure 11

**Evolution of pharmaceutical patents granted to domestic applicants, according to expiration date**



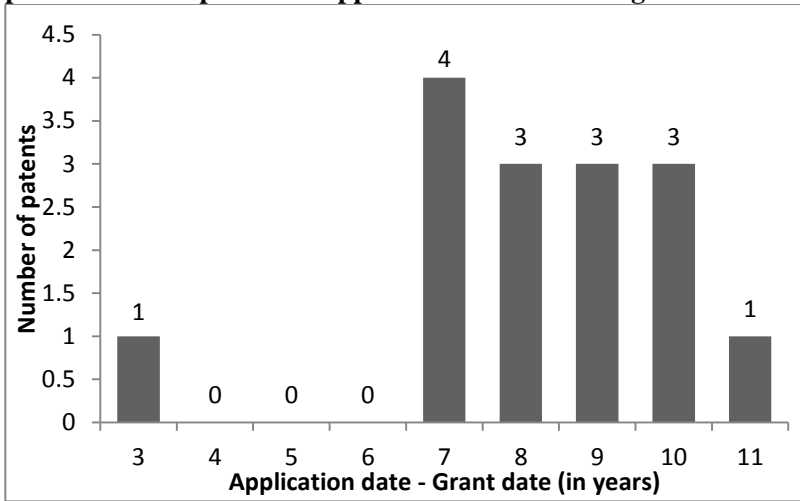
Source: Based on information published by INPI.

Figure 11 presents the expiration dates of the patents granted until 2007. Note that the majority of the patents will expire in 2017, while after that year the trend of patents expiring will decrease until arriving at one in 2024.

Figure 12 shows a histogram of the number of patents granted to domestic applicants by gap between year of application and grant. One may observe that the time lag is not homogeneous but oscillates between three and eleven years, and the average lag time is eight years.

Figure 12

**Gap existing between year of application and grant of pharmaceutical patents to applicants of domestic origin**



Source: Based on information published by INPI.

Concerning therapeutic uses, it is observed that there is no clear predominance of one type of use over others. However, topping the list with three granted patents are therapeutic uses for the Nervous System, followed by the Muscular-Skeletal system with two patents, while in third place there is a group of uses with one each.

It was not possible to confirm the therapeutic use for 5 patents which are indicated in the table as “undetermined”.

Table 8

**Therapeutic uses of patents of domestic origin**

Therapeutic use	Frequency	Percentage	Laboratories
Nervous system	3	20	SYNTEX S.A./BIO SIDUS S.A./ JOISON AGUSTIN NESTOR
Muscular-skeletal system	2	13	GADOR S.A./ BIOFARMA S.A.
Blood and hematopoietic organs	1	7	OUTOMURO, PABLO
Gastrointestinal tract and metabolism	1	7	BLANCO, GUILLERMO JAVIER, GIL
Systemic hormonal preparations, sex hormones and insulins	1	7	GADOR S.A.
Antiparasitics, insecticides and repellents	1	7	BIOGENESIS S.A.
Antiretroviral	1	7	BIOVACS INC
Undetermined	5	33	
<b>Total</b>	<b>15</b>	<b>100</b>	

*Source:* Based on information published by INPI.

Concerning the **type of claim** a clear predominance is observed of **product** claims, with 53 per cent (8 patents). See table 9.











Table 9

**Types of claims**




Type of claim	Frequency	Percentage
Product	8	53
Process	3	20
Product and Process	2	13
Product and Markush	2	13
<b>Total</b>	<b>15</b>	<b>100</b>

*Source:* Based on information published by INPI.

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## CHAPTER 3

### HEALTH, INTELLECTUAL PROPERTY AND INNOVATION POLICY: A CASE STUDY OF BRAZIL

Gabriela Costa Chaves\* and Renata Reis\*\*

#### I. THE PUBLIC HEALTH SYSTEM AND PHARMACEUTICAL POLICY IN BRAZIL

The 1988 Constitution of the Federal Republic of Brazil, also known as the “Citizen Constitution,” was brought into existence during Brazil’s re-democratization process, which had been intensifying since 1985. The “Public Health Movement” – dating back to the 1970s and comprised initially of healthcare professionals and students – played an essential role in the constitutional recognition that healthcare was a fundamental right. Article 196 of the Constitution established that “health is a right for all citizens and the duty of the State,” thus setting the foundation of the current public health system: the Unified Health System (SUS – acronym in Portuguese).

The challenge then was to establish a public healthcare system that conformed to the fundamental principles of universality, integrality,

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\* Pharmacist, Masters in Public Health (Oswaldo Cruz Foundation, Brazil) and Doctoral Candidate in Public Health (Oswaldo Cruz Foundation, Brazil).

\*\* Journalist and Lawyer, Masters in Social Policy and Doctoral Candidate in Public Policy, Strategies and Development (Federal University of Rio de Janeiro/Fiocruz).

The authors would like to thank Francisco Viegas Neves da Silva for his contribution on the topic related to intellectual property rights in part I of the study and to Prof. Lia Hasenclever for the review of the first draft of the part I, providing sensitive input for the improvement of the content.

and equal access to healthcare services for prevention and treatment, Laws 8.080/90 and 8.142/90 regulate the SUS. The first established the principles of decentralization of actions and services in healthcare and its management at the municipal level. Moreover, it further defined the interaction between federal, state, and municipal administrations. The latter law facilitates a means for society to participate in the administration of the system through municipal, state and federal health councils as well as through related aspects of intergovernmental transfer of resources within the SUS (Marín, 2003).

The SUS provides integrated therapeutic services, including pharmaceutical services, which means that the State has a duty to provide medicines to all that are in need.

In 1998, the National Medicine Policy (PNM – acronym in Portuguese) was approved by Ordinance 3.916/98. As a component of the national health policy, it sought to establish a government strategy to promote access to medicines. It guaranteed competition within government generated programmes, projects and activities and aimed to reduce potential discontinuities among inter-governmental activities.

The main objectives of the PNM are to guarantee the safety, efficacy and quality of medicines, to promote their rational use and to ensure the population's access to essential medicines.

The PNM establishes a series of guidelines and priorities (indicated in Table 1). Examples of concrete actions can be found in the most recent version of the National List of Essential Medicines (RENAME – acronym in Portuguese; 6th edition), which has been employed by the Brazilian government since 1964 (Silva and Bermudez, 2004). The Ministry of Health also created the National Therapeutic Form<sup>1</sup> (2008) as a supplement to RENAME with the same list of medicines contained in 2006, in order to ensure the availability of evidence-based information for healthcare professionals.

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<sup>1</sup> Available on the electronic page of the Ministry of Health <http://portal.saude.gov.br/portal/arquivos/multimedia/paginacartilha/iniciar.html>.

Table 1

**Guidelines and priorities in the national medicine policy – 1998**

<b>Guideline</b>	<b>Priority</b>
Adoption of the National List of Essential Medicines (RENAME)	Permanent Revision of RENAME
Sanitary regulation of medicines	
Reorientation of pharmaceutical healthcare to not restrict the purchase of medicines; rather to cover activities related to the promotion of access to essential medicines	Pharmaceutical services
Promotion of the rational use of medicines	Promotion of rational use of medicines (educational campaigns, registration and use of generic medicines, National Therapeutic Form, pharmacoepidemiology and drug safety, human resources)
Scientific and technological development	
Promotion of medicine production	
Guarantee of safety, efficacy and quality of medicines	Organization of activities of health surveillance of medicines
Development of capacity of human resources	

In 2004, the National Health Council (CNS – acronym in Portuguese)<sup>2</sup> approved the now-called Pharmaceutical Services Policy – Resolution CNS 338/2004, which strengthened the scope of the PNM and established principles such as:

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<sup>2</sup> The National Council of Health is a body of a permanent and deliberative character, a component of the structure of the Ministry of Health, composed of government representatives, workers in the service and healthcare sectors, and patients.

“...the **Pharmaceutical Services Policy** must be understood as a guiding light for the creation of sectoral policies such as the **policies for medicines, science and technology, industrial development** and the formation of human resources. These guarantee, among other things, the inherent interaction of sectors of the Unified Health System (SUS), whose implantation involves as much the public sector as the private sector in regards to healthcare” (BRASIL, 2004a).

Marketing approval of medicines in the country is conducted by the Brazilian Health Surveillance Agency (ANVISA – acronym in Portuguese), under Law 6.360/76 and Law 9.787/99. According to these laws, the data and results from clinical trials of medicines that are under tentative approval are protected from antitrust law. The unauthorized use of these results is even punishable under criminal law (Article 195, Item XIV of the Industrial Property Law). Currently, ANVISA publishes marketing approval lists of only the medicines that have been approved.

It is worth mentioning that public procurement of medicines is made at the three State levels. Some medicines are provided under specific programmes, such as the Basic Pharmaceutical Service (medicines provided in the primary health care). Strategic Medicines include antiretrovirals for HIV/AIDS, tuberculosis, leprosy, blood products, diabetes and endemic control (medicines for Chagas disease, schistosomiasis, filaria, leishmaniasis, malaria etc.) (OPAS/OMS/Brasil, 2005).

Although important achievements have been made with the implementation of the pharmaceutical policy in Brazil, it is important to emphasize that access to lifesaving medicines is an on-going challenge, given the persistence of different constraints. For this reason, since the publication of the current Constitution, patients have also resorted to courts to demand access to medicines, such as, medicines unavailable at the public health facilities or for medicines not incorporated into the public treatment protocols (Figueiredo et al, 2010). In the case of some antiretrovirals (ARVs), for the past years, several shortages of abacavir,

nelfinavir, atazanavir, lamivudine, nevirapine have been reported in the country (Jornal O Estado de São Paulo, 2010, 2011).

## **I.1 The Policy of Generic Medicines**

The approval of Law 9.787/99, commonly known as the Law of Generic Medicines, was an important outcome of the PNM policy. After the approval of this law, the Brazilian pharmaceutical market is composed of ‘reference medicines’ (brand medicines), ‘generics’ and ‘similar medicines’.

The essential difference between generic medicines and similar medicines is their interchangeability with the originator’s product (reference medicine). As indicated in the Law, interchangeability denotes the possibility for a user to substitute a reference-listed drug for a corresponding generic. It is, however, necessary that the generic product be subjected to tests of bioequivalence and be presented to the Brazilian drug regulatory authority. Moreover, generic medicines are designated by the name of the active ingredient, in accordance with the Brazilian Non-proprietary Name (DCB – acronym in Portuguese), or, in its absence, the International Non-proprietary Name (INN).

Similar medicines have been present on the market even before the adoption of the Law of Generic Medicines. They compete with reference-listed drugs and generics, but are not interchangeable with reference-listed drugs since they have not undergone tests of bioequivalence. They are identified by the compounds, brand name or trademark. Since 2003, ANVISA required that all similar medicines, upon renewal of market approval (registration), be submitted to tests of pharmaceutical equivalence and relative bioavailability (bioequivalence) to the reference medicines. The legislation for market approval of similar medicines has aimed at gradually achieving the same requirements for the registration of generic medicines (ANVISA, 2003, 2007).<sup>3</sup>

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<sup>3</sup> According to ANVISA, “the submission of tests of relative bioavailability for similar medicines already registered follows an order of priority, which in other words means medicines considered as high risk, such as antibiotics, antineoplastics (anti-cancer), antiretrovirals and other medicines with active ingredients that have

The Law of Generic Medicines established in its third article that "...the procurement of medicines, under whichever method of purchase, as well as medical prescriptions and odontological medicines, under the domain of the SUS..." must obligatorily adopt the DCB, or in its absence, the INN.

The Law also establishes that – in accordance with the Public Tender Law (Law 8.666/93) – the public procurement of generic medicines, when existing on the market, have priority over other competing medicines in case of equal pricing.

Although the generic market is growing considerably (as will be shown in the next section) and there is an evident stimulus that comes from the pharmaceutical policy, this does not necessarily mean that the public sector is benefiting from this environment.

A recent study (Miranda *et al*, 2009) investigated the availability of generic medicines in the public sector and their price in the private sector by applying the prices reported by the World Health Organization (WHO) and Health Action International (HAI) (WHO and HAI, 2003) in the Brazilian context.

In 2007, the prices and availability of 43 medicines were evaluated, of which 18 were selected from RENAME or from at least three programmes of the Ministry of Health, taking therapeutic indications for high prevalence diseases in Brazil into account. Of the total evaluated, only 65.1 per cent (28) had generic versions already registered in Brazil, 24 of which were included in RENAME 2006.

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already shown this compliance in the first renewal after the publication of this resolution (RDC 133/03 and 134/03). Other medicines will have to submit tests of relative bioavailability in the second renewal of registration, and by 2014 all similar medicines should have complied with the relative bioavailability requirement". Available from:

[http://portal.anvisa.gov.br/wps/portal/anvisa/home/medicamentos?cat=Medicamento+s+similares&cat1=com.ibm.workplace.wcm.api.WCM\\_Category%2FMedicamentos+similares%2F75c46e804f6be6adaf5fbfc894994279%2FPUBLISHED&con=com.ibm.workplace.wcm.api.WCM\\_Content%2FMedicamento+Similar%2F451ca080401a4c5db113b754e035b7cb%2FPUBLISHED&showForm=no&siteArea=Medicamento+s&WCM\\_GLOBAL\\_CONTEXT=/wps/wcm/connect/anvisa/Anvisa/Inicio/Medicamentos/Publicacao+Medicamentos/Medicamento+Similar](http://portal.anvisa.gov.br/wps/portal/anvisa/home/medicamentos?cat=Medicamento+s+similares&cat1=com.ibm.workplace.wcm.api.WCM_Category%2FMedicamentos+similares%2F75c46e804f6be6adaf5fbfc894994279%2FPUBLISHED&con=com.ibm.workplace.wcm.api.WCM_Content%2FMedicamento+Similar%2F451ca080401a4c5db113b754e035b7cb%2FPUBLISHED&showForm=no&siteArea=Medicamento+s&WCM_GLOBAL_CONTEXT=/wps/wcm/connect/anvisa/Anvisa/Inicio/Medicamentos/Publicacao+Medicamentos/Medicamento+Similar)

Of these 28 medicines, 10 were not found in their generic version in any region of Brazil. According to the authors, 64.8 per cent of the active ingredients included in RENAME did not have generic versions available in the country. This demonstrated a disconnection between the policy of generic medicines and the list medicines – the integration of which is one of the objectives of the PNM.

The study found that the availability in the region studied, was proportionally less for generic versions than the reference-listed drugs. Moreover, it observed that there were more similar medicines than there were generics in the public sector in all regions of Brazil. Regions like the Southeast and South accounted for the biggest number of available generic medicines, 53.6 per cent and 32.1 per cent respectively.

## **I.2 The Programme of Popular Pharmacy – A Case of Co-payment**

The Brazilian Programme of Popular Pharmacy (PFPB – acronym in Portuguese) was launched in 2004, by the federal government as a co-payment system, based on the articulation of the public and private sectors. It aimed to increase access to medicines in Brazil by the population that did not employ the SUS, by making available a set of medicines whose costs were subsidized by as much as 90 per cent. It presented itself as a new strategy adopted in the backdrop of the PNM.

The dispensing units of the Popular Pharmacy can be categorized as follows: a) units of the Oswaldo Cruz Foundation (Fiocruz); b) units established in partnership with Fiocruz (municipalities/secretariats of health) or through agreements with public and private entities and institutions in the non-profit sector, health assistance or higher education; c) private pharmacies, supporters of the Programme (under coordination of the Ministry of Health) (Santos-Pinto, 2008).

From its inception in June 2004, the number of dispensing units grew greatly, up to 407 units in 2007 (SANTOS-PINTO, 2008). The list of medicines of the PFPB includes 107 items, 76 of which are also included in RENAME 2006 and 12 in RENAME 2002. In terms of the



therapeutic profile of the products, 25 per cent are disinfectants, 12 per cent are medicines for the central and peripheral nervous system and 12 per cent are for the cardiovascular and kidney systems (Santos-Pinto, 2008).

Santos-Pinto further asserts that 70 per cent of medicines in the PFPB are also part of the programmes of the Ministry of Health (MS – acronym in Portuguese), in as much as both are pertinent to RENAME and to the most prevalent health conditions in the country. This suggests that PFPB is an option for the procurement of medicines both for the users of the private healthcare system and for users of the public healthcare system.

## **II. PUBLIC SPENDING ON HEALTH AND MEDICINES IN BRAZIL**

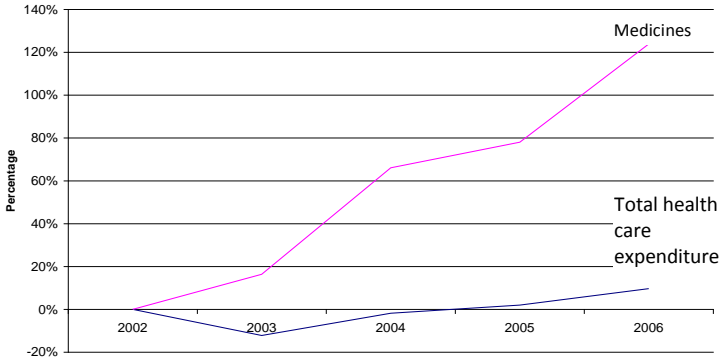
Public spending on health, and specifically on medicines, has grown significantly in terms of importance in various developing countries. According to the Organization for Economic Cooperation and Development (OECD), the average expenditure on healthcare made up 7 per cent and 8.9 per cent of the Gross Domestic Product (GDP) in 1990 and 2004 respectively for member countries. Brazil also follows this trend.

A study realized by Viera & Mendes (2007) demonstrates that between 2002 and 2006 healthcare spending by the Ministry of Health increased 9.6 per cent while spending on medicines increased 123.9 per cent<sup>4</sup> for the same period (see figure 1).

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<sup>4</sup> The authors emphasize that this calculation does not include expenditure for the Brazilian Programme of Popular Pharmacy and the funding for anti-neoplastics.

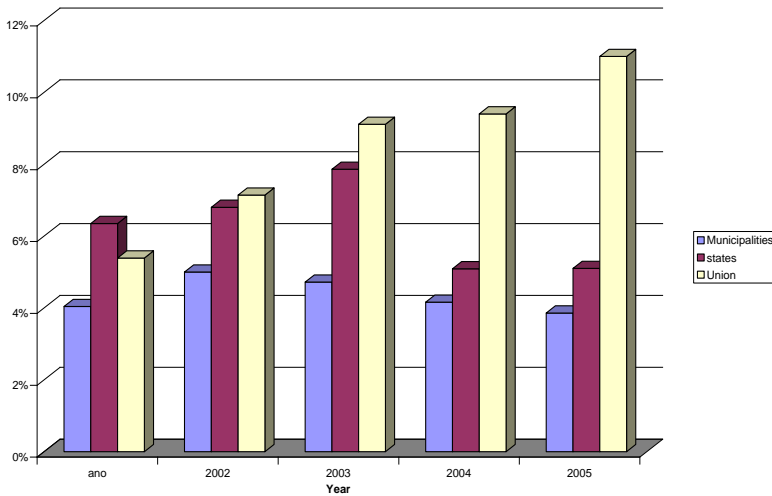
**Figure 1**  
**Evolution of total expenditure (percentage) on health care and medicine by the Ministry of Health, 2002-2006**



Source: Vieira & Mendes, 2007.

Vieira and Mendes point out a few reasons for the significant increase in spending on medicines: a) the organization of pharmaceutical services since the approval of the PNM; b) pharmaceutical services for high complexity healthcare, was responsible for a considerable increase in medicines expenditures, from 516 million Reals (Brazilian currency) in 2003 to 1.3 billion reais in 2006, representing an increase in real terms in the order of 150 per cent; c) the increase in spending on antiretrovirals jumped from 611.8 million reais in 2003 to 924.8 million reais in 2006 (an increase of 51.1 per cent), with a 28.7 per cent increase in the number of patients being treated for the same period. The spending on medicines at federal, state and municipal levels (see figure 2), indicates that the biggest contributions were made at the federal level and increased from 5.4 per cent in 2002 to 11 per cent in 2006. Vieira and Mendes suggest that, between 2002 and 2005, municipalities and states also raised their spending on health services considerably – 66 per cent and 50 per cent respectively.

Figure 2

**Evolution of municipal, state and federal expenditures (percentage) on medicines in relation to total spending on health, 2002-2006**

*Source: Vieira & Mendes, 2007.*

Since the figure refers to the budget for medicines, it is worth considering briefly the panorama presented by the Family Budget Research (POF – acronym in Portuguese), carried out by the Brazilian Institute of Geography and Statistics (IBGE – acronym in Portuguese) during the years 1995-1996 and 2002-2003.<sup>5</sup> This research seeks to detail the way in which Brazilian families spend on categories such as healthcare, food, transportation, clothing, hobbies, etc.

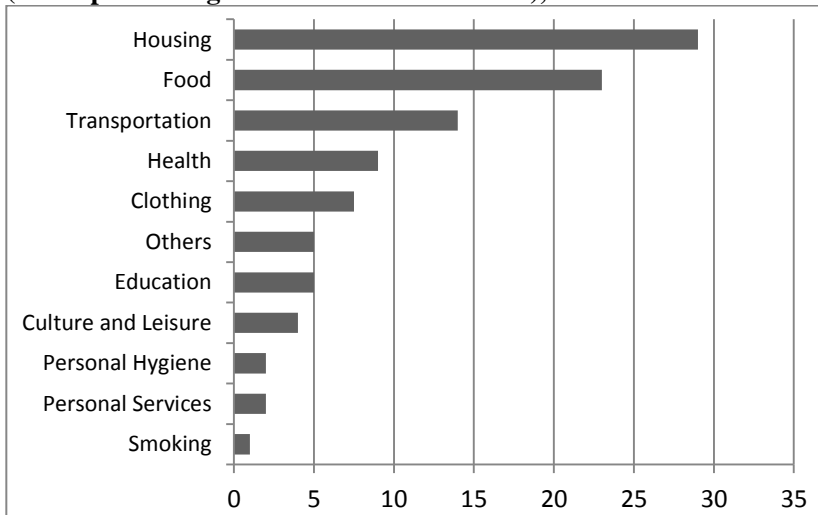
The information from the POF allows us to evaluate expenditures for healthcare in relation to other types of family expenditures. Of the total disbursement of resources by families covered by the POF from 1995 to 1996, 81 per cent were destined to current expenditures, 17 per cent to assets and the remaining 2 per cent to the

<sup>5</sup> The POF 1995-1996 covered nine metropolitan regions of the country (São Paulo, Rio de Janeiro, Belo Horizonte, Salvador, Recife, Fortaleza, Belem, Curitiba and Porto Alegre), the Federal District and Goiania. The POF 2002-2003 illustrates a sample that allows for the evaluation of Brazil in large regions, considering both urban and rural areas (Menezes *et al*, 2006).

decrease of liabilities. Of the current expenditures, 88 per cent are expenditures on consumption (71 per cent of the global disbursement).

Figure 3 represents the distribution of consumption expenditures according to various groups. Spending on healthcare represents 9 per cent of these expenditures (7 per cent of the global disbursement), being the fourth largest item in family expenditures, after only those on shelter, food and transportation. This ranking indicates that healthcare expenditures place a significant burden on families' budget. It should be emphasized that the population covered by the POF was equivalent in 1996 to 30 per cent of the Brazilian population and 38 per cent of the Brazilian urban population (Silveira *et al*, 2002).

Figure 3  
**Health care expenditures as a percentage of families' consumption (Metropolitan regions. Brasilia and Goiania), 1995-1996**



Source: SILVEIRA *et al*, 2002.

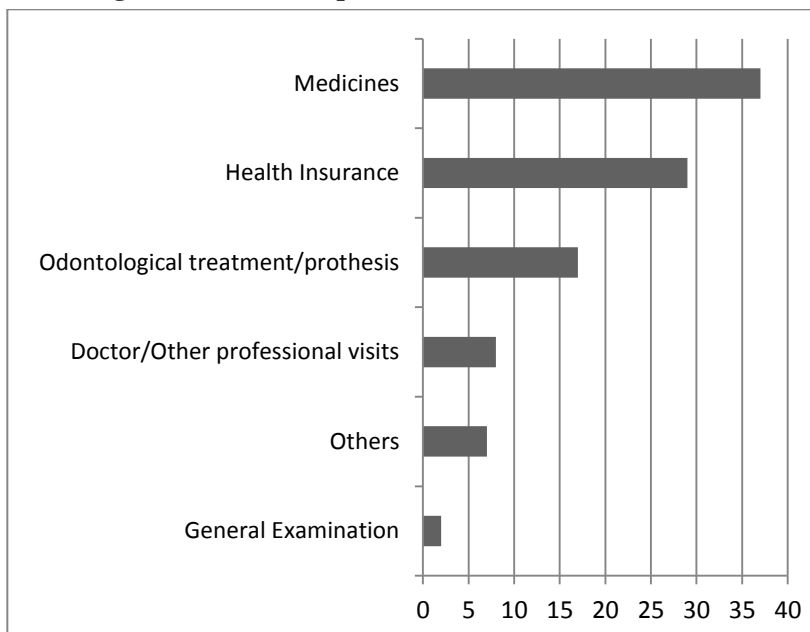
When healthcare spending is detailed for Brazilian families, medicines and healthcare insurance account for the biggest slice (figure 4). Moreover, the study shows that for the poorest population, spending on healthcare is in its totality accounted for by expenditures on medicines, while in the richest part of the population healthcare

insurance becomes a focus. Silveira *et al.* (2002) emphasize that in 48 per cent of cases in which a medicine is prescribed for the people that make up 20 per cent of the poorest part of the population, the medicine is freely provided by the public health system.

The analysis on health expenditure in the POF 2002-2003 reached similar conclusions (Menezes *et al.*, 2006).

Figure 4

**Percentage of healthcare expenditures for families, 1995-1996**



*Source: Silveira et al., 2002.*

### **III. THE MARKET OF GENERIC MEDICINES IN BRAZIL**

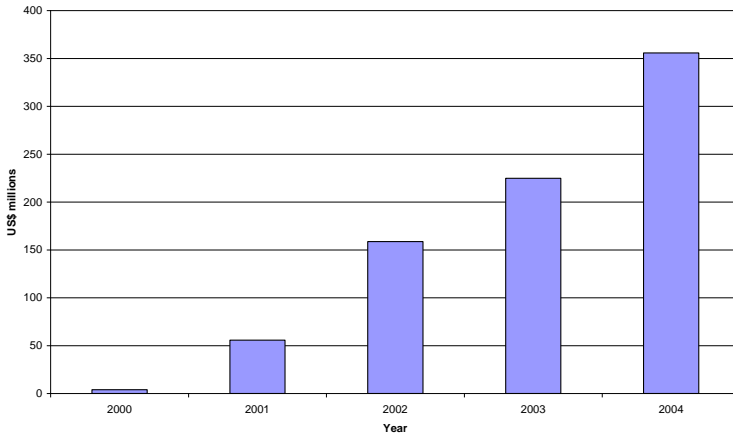
In 2008, twelve countries were responsible for 80 per cent of the world pharmaceutical market, totalling US\$560 billion. Brazil occupied the tenth position with a market estimated at US\$13.4 billion or the

equivalent of 1.6 per cent of the world pharmaceutical market (INTERFARMA, 2009).

The pharmaceutical industry in Brazil is composed of private domestic and foreign corporations as well as public entities. They are organized in various associations, depending on whether they are funded from domestic or foreign capital and on the types of products produced (intermediaries, active ingredients and/or final products).

After the adoption of the policy on generic medicines, their market expanded significantly. In the period 2000-2004, it grew from US\$4 million to US\$355.6 million – as shown in figure 5 (Fardelone and Branchi, 2006).

**Figure 5**  
**Annual development of the generic market in Brazil, 2000-2004**



*Source:* Fardelone and Branchi, 2006.

Hasenclever and Paranhos (2008) note that in 2004, generic medicines represented 5.3 per cent of the market of medicines in Brazil and 11.4 per cent in 2006. By September 2009, generic medicines already represented 19.6 per cent of the units purchased on the Brazilian pharmaceutical market (IMS-HEALTH in PRÓ-GENÉRICOS, 2009).

In 2008, approximately 91 per cent of the Brazilian generic market was dominated by only eight companies, five of which were Brazilian: Medley, EMS, Sigma Pharma, Ache/Biosintetica and Eurofarma in the first five positions and, Germed, in the seventh position. In the sixth position was the Indian company Ranbaxy. Medley and EMS have occupied the first and second positions, respectively, since 2001 until now, and by 2008 they represented 60.8 per cent of the generic market (Rosenberg, 2009).

In terms of the number of medicines with marketing approval for generics granted by ANVISA, 89 per cent come from domestic companies and laboratories, 21 per cent are registered by foreign companies, 63 per cent of which are accounted for by Indian companies (data updated on 20 November 2009) (ANVISA, 2009).

#### **IV. RECENT POLICIES ON INNOVATION IN BRAZIL AFFECTING THE PHARMACEUTICAL SECTOR**

The policy for science and technology in Brazil is defined at the federal level, by the Ministry of Science and Technology (MCT – acronym in Portuguese). Although local states and municipalities intervene in important issues, the federal government determines policies such as, the selection of priorities and the establishment and supervision of federal universities. Nevertheless, as discussed in this chapter, various incentives and policies for the development of innovation in the pharmaceutical sector are influenced by other governmental ministries like the Ministry of Development, Industry and Foreign Trade (MDIC – acronym in Portuguese) and the Ministry of Health (MS – acronym in Portuguese).

In conjunction with the two most important development agencies in the country (FINEP and the CNPq) and their branches of research, the MCT<sup>6</sup> coordinates programmes and actions to complement the National Policy on Science, Technology and Innovation.

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<sup>6</sup> In addition to the agencies of development, the system of the MCT consists of: the Center of Administration of Strategic Studies (CGEE – acronym in Portuguese); the

Around the world, healthcare is an area that demands significant public and private resources for research. In Brazil, between 2002 and 2008, the average annual expenditure on healthcare R&D was US\$573 million (including all universities, institutions with activities in healthcare research, the MS, the MCT (with its agencies of development) and the Ministry of Education, in addition to the main R&D state agencies ) (Guimarães, 2006).

A strategy utilized by the MS in conjunction with the MCT is the establishment of priorities to improve and harmonize ministerial policies in health-related research (Marziale, 2004).

In this light, the National Policy for Science, Technology and Innovation in Health (PNCTIS – acronym in Portuguese) was developed as an integral part of the National Policy on Health, which in turn was formulated in the framework of the Unified Health System (SUS). Article 200(5) of the Federal Constitution establishes the jurisdiction of the SUS, including scientific and technological development in healthcare.

It is important to remember that the SUS has three fundamental constitutional principles: universality, integrality and equality. PNCTIS must also comply with these three principles. According to the document which establishes PNCTIS:

“an application of these principles must correspond with the political and ethical commitment to production and to the acquisition of knowledge and technology that contribute to reduce social inequalities in health, allied with the social control”  
(translated by the authors).”

The national system of innovation in healthcare can be characterized as an economic, political and institutional construct, where

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National Commission of Nuclear Energy (CNEN – acronym in Portuguese); the Brazilian Space Agency (AEB); 19 units of scientific, technologic and innovative research; and four state companies: Brazilian Nuclear Industries (INB); Nuclebrás Heavy Equipment (Nuclep); Alcântara Cyclone Space (ACS) and the Center of Excellence in Technology and Advanced Electronics (Ceitec).



diverse interests converge, including those of the private and public companies, institutions of S&T and civil society. This construct relies on the interaction between the national system of innovation and the healthcare system (Gadelha, 2003).

Although a policy of active investments in the scientific and technological infrastructure has already started, which is practically unique in Latin America (BERMUDEZ, 1992, 1995), there were inconsistencies in the incentives for private investments for innovation. Since the middle of the current decade, Brazil has incorporated into its legislation a significant number of support instruments for innovation, in accordance with the Industrial, Technological and Foreign Trade Policy of the Federal Government (PITCE – acronym in Portuguese).<sup>7</sup>

Several strategies are being developed, such as: fiscal incentives for company innovation (Law of Well-being – 11.196/2005); loans; government procurement; direct subsidies to companies (Law of Innovation – 10.973/2004); special incentives for new technology-based companies, small, medium and big companies; support to public research institutions and facilitation of cooperation between public institutions of science and technology (ICTs – universities, technological institutes etc.). It is worth highlighting that the PITCE provides for the strengthening of the intellectual property system in the country.

Due to the impossibility of detailing all aspects of the PITCE in an exhaustive manner, this chapter describes two instruments that have been useful in promoting innovation and which may have an important role in the pharmaceutical sector: the Law of Well-being and the Law of Innovation. It will also briefly describe the launch of the so-called “health industrial complex” in 2008, aimed at reducing the dependence on importation of medicines and at using the purchasing power of the

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<sup>7</sup> PITCE guidelines were launched on 26 November 2003. On 31 March 2004, at the headquarters of the National Confederation of Industry, it was complemented by an event which brought together the President of the Republic, various State ministers, presidents and directors of diverse public institutions, like BNDES, Banco do Brasil, Caixa Econômica Federal, Ipea, Apex, FINEP 2004. This event was considered one of the biggest meetings of Executive authorities for the launching of a government programme (Salerno and Daher, 2006).

government to stimulate local production and strengthen its regulatory role in the market.

#### **IV.1 Law 11.196/2005 – The “Law of Well-being”**

In 2005, Law 11.196, commonly known as the “Law of Well-being”, came into force. It introduced fiscal incentives for companies that invested in R&D.<sup>8</sup> These incentives were given to those companies that did not need previous approval from the MCT. The law was subsequently altered by law 11.487 on 15 June 2007. Fiscal incentives for companies that had completed research and developed technological innovation were listed.

The Law of Well-being introduced such fiscal incentives as: the reduction of Excise Tax on Industrial Products (IPI – acronym in Portuguese) on the purchase of equipment destined for R&D; credit on income taxes, delayed pay-as-you-earn taxes on remittances abroad of royalties related to technical and scientific assistance and services for R&D; reduction to zero of the rate of income tax for withheld remittances for the registration and maintenance of trademarks, patents and plant varieties.

In addition to fiscal incentives, economic subsidies were established in the contracts of masters’ and doctoral researchers involved in research and technological innovation.

#### **IV.2 The Law of Innovation**

In 2004, Law 10.973, more commonly known as the “Law of Technological Innovation” (LIT – acronym in Portuguese) was enacted.

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<sup>8</sup> The Programme of Industrial Technological Development (PDTI – acronym in Portuguese), established by Law 8.661/1993 and revoked by the Law of Well-being, demanded the submission of a formal project proposal to the MCT concerning the development plans of the company. The proposal would then be analyzed by the MCT’s technical team, which would, after approving the proposal, inform the *Receita Federal* – the federal taxing service – that the company completed the Law’s incentive. (Salerno and Daher, 2006).

The LIT established a mechanism of incentives for innovation, scientific and technological research in a productive setting, aiming at improving the capacity, technological autonomy and industrial development of the country, in accordance with articles 218 and 219 of the Federal Constitution.

The Law is organized around three main targets: to build up an environment for partnerships between universities, technological institutes and businesses; to stimulate the participation of institutions of science and technology in the innovation process; and to incentivize innovation within the private sector.

The LIT established, among other things, a means to galvanize public science and technology institutions to license inventions without public bidding: flexibility for researchers of public ICTs to get away from work in order to collaborate with other ICTs, or develop corporate innovative activity; and the creation of methods of financial support through direct economic subsidies for businesses, with the objective of generating product and process developments.

In order to implement this law, the federal government created the Brazilian Agency for Industrial Development – ABDI (Matias-Pereira and Kruglianskas, 2005). ABDI is connected with the MDIC, and has the mission to promote the Brazilian Industrial Policy.<sup>9</sup>

### **IV.3 PROFARMA**

To better understand the incentive policies for pharmaceutical innovation in Brazil, it is necessary to consider the initiatives undertaken in the context of the MDIC in conjunction with the MS.

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<sup>9</sup> The ABDI also acts as the Executive Secretary of the National Council of Industrial Development – CNDI and of the National Committee of Biotechnology. In addition to these activities, ABDI develops five micro-programmes that mobilize and put together development entities, academics, representatives of the private and government sectors, to definite strategies that promote industrial competitiveness through innovation, with a focus on transversal dissemination of new technologies and the international insertion of Brazilian companies. Source: ABDI.

After decades of inactivity, the Brazilian government opened the debate on the development of the pharmaceutical sector in the country. In May 2003, the Competitiveness Forum on the Pharmaceutical Productive Chain was established under the coordination of the MDIC and the MS. In March 2004, the MDIC launched the PITCE. The pharmaceutical industry was among the strategic areas identified by the PITCE.

This process led to the establishment of the Support Programme for the Development of the Pharmaceutical Productive Chain (PROFARMA) of the National Bank of Economic and Social Development (BNDES), from May 2004 to December 2007, thereafter renewed until 2012.

The objectives of PROFARMA are: a) to encourage the production of medicines and their consumption in Brazil; b) to improve the quality of medicines produced for human use and their adequacy to meet the demands of national regulatory agencies; c) to reduce the trade deficit of the pharmaceutical productive chain; d) to facilitate research activities, pharmaceutical development and innovation in the country; and e) to strengthen the economic, financial, commercial and technological position of domestic companies.<sup>10</sup> Table 2 indicates the projects approved by BNDES in 2004-2007.

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<sup>10</sup> PROFARMA 2004-2007 was divided into three sub-programmes: 1) PROFARMA Production: investments for the implantation, expansion and/or modernization of productive capacity and compliance with regulatory standards set by ANVISA and international agencies; 2) PROFARMA R, D & I: investments in research, development and innovation; and; 3) PROFARMA strengthening of national companies: support of incorporations, acquisitions and mergers of companies in order to create companies under national control.

Table 2

**Distribution of PROFARMA budget for its sub-programmes**

<b>Sub-programme</b>	<b>Number of projects</b>	<b>Total value of projects (in R\$ millions)</b>	<b>Value of support from the BNDES (in R\$ millions)</b>
Production	34	1,277.6	568.2
R, D & I	13	156.7	112.2
Fortification of National Companies	2	564.3	345.7
<b>Total</b>	<b>49</b>	<b>1,998.6</b>	<b>1,026.2</b>

*Source:* GSET/DEFARMA/BNDES.

In total, 49 projects were approved, the majority in the subarea of production, for the renovation, conservation or building up of pharmaceutical production capacities. According to an analysis from the BNDES, the majority of projects on research, development and innovation refer to incremental innovations, such as the developments of fixed dose combinations, studies for the second use of already-existing medicines, formulations for controlled liberation, and scientific evaluation of traditional knowledge (Capanema *et al*, 2008).

#### **IV.4 The Industrial Health Complex**

In 2008, the so-called Industrial Health Complex was launched (CIS – acronym in Portuguese). The concept of CIS seeks to marry the healthcare and economic sectors, by promoting the linkage between healthcare and development (Gadelha, 2003, 2005, 2006). It is an ambitious partnership with inherent tensions; it aspires not only to provide adequate healthcare to all Brazilians (which in itself is a challenge), but also to reduce foreign dependency in strategic areas such as medicines and the restructuring of the national production base. Table 3 sheds light on the current situation, goals and challenges of the CIS.

Table 3

**Current situation, goals and challenges for the Industrial Health Complex**

<b>Current situation</b>	<b>Goals</b>	<b>Challenges</b>	<b>Programme management</b>
-The productive health chain represents 7% to 8% of the GDP( R\$160 billion) -Strong dependence on imports that require higher knowledge and technology -High trade deficit: US\$ 5.5 billion in 2007	-Reduce the trade deficit of the CIS to US\$4.4 billion by 2013 -Develop technology for local production of 20 strategic products for the SUS by 2013	-Decrease the vulnerability of the National Health Policy -Increase innovation investment -Increase and diversify exports -To boost the CIS productive chain and strengthen national companies -To strengthen, expand and modernize the network for management of public laboratories -To attract R&D and production by foreign companies	Ministry of Health

*Source:* MDIC.

The CIS refers to a set of challenges and establishes a set of instruments (institutions, legislation, funding etc.) to respond to each of them. Some of the actions foreseen under the CIS include a) the use of the government purchasing power to stimulate local production, b)

funding for increasing the production capacity, c) expand resources for R&D in strategic areas, d) creation of networks for technological and industrial development (Guimaraes, 2008).

PROFARMA was renewed (2007-2012) following strategic guidelines to promote CIS competitiveness, to contribute to the reduction of the vulnerability of the National Health Policy and to articulate the PITCE with a healthcare policy.<sup>11</sup> The total approved budget for the programme was R\$ 3 billion, limited to R\$ 1 billion annually.<sup>12</sup> The programme will end on 31 July 2012.

One interesting tool adopted in the context of CIS through Inter-ministerial Ordinance 128/2008 and Ordinance 3031/2008. The first establishes guidelines for the public procurement of medicines and drugs by the SUS, with the following priorities:

1) Purchase of medicines: preference will be given to national tenders, which should, as a prerequisite, submit the certificate of marketing approval and the certificate of good manufacturing practices, issued by ANVISA. They should also submit a declaration of the

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<sup>11</sup> PROFARMA is divided into five subprogrammes: a) Profarma-Production: support for projects related to construction, expansion or modernization of productive capacity; internationalization of national companies; investments needed to meet national and international regulatory demands; and initiatives directed towards the improvement or modernization of the organizational, administrative, commercial, distribution and logistical structure of the company; b) Profarma-Exports: support for the production of goods in the CIS for export and for the foreign commercialization of medical appliances and machines and odontological equipment developed in Brazil and associated services, c) Profarma-Innovation: support for innovative projects, with or without cooperation with scientific and technological institutions, as well as for investments related to the consolidation of the health-related innovation infrastructure in the country; d) Profarma-Restructuring: support for the incorporation, acquisition or consolidation of companies that result in the creation of companies of domestic capital of greater size and/or more vertical companies; e) Profarma-Public Producers: the first phase consists of a study to elaborate a strategic plan for insertion of public producers in the National Health System. The second phase consists of implementing the results emerging from the first phase.

<sup>12</sup> For the subprogramme Profarma-Innovation, there is an annual disbursement limit of R\$ 300 million through financing and R\$ 100 million through the participation in the results of the project (Capanema *et al.* 2008).

producer, which shall be subject to verification, referring to the origin of the finished product and its active pharmaceutical ingredient. With regard to patented products not produced in Brazilian territory, after the third year of the patent, a compulsory license may be issued (as it is established in the article 68, item I, § 10 § 5, item II, of Law 9.279 of 1996).

2) Purchase of active pharmaceutical ingredients by public laboratories: one of the requirements for participating in a public tender is the existence of a production site in the national territory, and the contractor's right to make direct inspections of the contracted processes, quality, traceability, customization and optimization of the entire production process and of the product. If such products are not available in Brazil and their supply requires the participation of foreign companies in the tender, mechanisms should be created to ensure product quality before its internalization in the country.

Ordinance 3.031/2008, moreover, complements the tender rules for APIs by public manufactures, as follows:

- Preference will be given to the acquisition of API from companies that produce API domestically.
- When there is more than one producer of a certain API in the country, preference should be given to the producer with the highest level of vertical production in the country.

As an example of the results of these measures, a compulsory license for the medicine efavirenz was issued in 2007 (this will be discussed below), whose national production by Farmanguinhos (FIOCRUZ) relied on the possible acquisition of the API from domestic private companies (Globe, Cristália and Nortec). The domestic version of the medicine was launched in February of 2009.

In addition to these tools that provide preference for API acquisition, the government issued Ordinance 978/2008 (updated by Resolution GM/MS No. 1284/2010), which established a list of strategic medicines for the SUS with the goal of supporting the industrial policy. Among the 101 items listed, 13 were ARVs.<sup>13</sup>

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<sup>13</sup> Atazanavir, didanosine, efavirenz, enfuvirtide, indinavir, lamivudine, lopinavir, nevirapine, ritonavir, tenofovir, saquinovir, saquinovir mesilate, zidovudine.



Another important recent result is the national development of tenofovir (TDF), whose patent application filed by the US company Gilead was denied in 2009 (see details below). Two public-private partnerships were established involving two official laboratories for the production of the final product: Farmanguinhos with Globe and FUNED, with Nortec and Blanver (Hasenclever, 2009).

From November 2009 to May 2010, seventeen agreements were established to locally produce 22 strategic products in order to substitute the importation. Economic savings were estimated at R\$170 million/year (around US\$100 million) for 5 years.<sup>14</sup>

It is too early to assess the effects on the health sector of the policies implemented under CIS. One important issue to be raised relates to transparency of the agreements between public and private manufacturers and the Ministry of Health, as well as how the costs are defined and prices of the final products established for the government.

For example, at the beginning of February 2011, newspapers<sup>15</sup> announced a public-private partnership, funded by the Ministry of Health, for the antiretroviral tenofovir (TDF), between Nortec (domestic private manufacturer of API) and FUNED (public manufacturer of the final product). According to a statement made by the head of CIS, the current price to be paid by the MoH was R\$4.02 per tablet, with the commitment to reduce it to R\$3.06, with potential savings by 2014 of R\$410 million.

Considering the price of R\$4.02 (US\$2.41 on 10 February 2011), the cost of the treatment per patient per year would be

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<sup>14</sup> Interview with the Head of the Department of Science, Technology and Strategic Products from the MoH Reinaldo Guimaraes. 2010. See also, *Acordo para a produção nacional de medicamentos promove a criação de empregos e o desenvolvimento tecnológico da indústria*. Revista. Available from [http://www.odisseu.com.br/Acesso/newsletter/107\\_03junho2010/index.html](http://www.odisseu.com.br/Acesso/newsletter/107_03junho2010/index.html). Accessed on 3 June 2010.

<sup>15</sup> “Governo passará a fabricar remédio contra Aids que era importado dos EU”, *Correio Braziliense*, 10 February 2011. Available from [http://www.correio braziliense.com.br/app/noticia/brasil/2011/02/10/interna\\_brasil,237010/governo-passara-a-fabricar-remedio-contr-aids-que-era-importado-dos-eua.shtml](http://www.correio braziliense.com.br/app/noticia/brasil/2011/02/10/interna_brasil,237010/governo-passara-a-fabricar-remedio-contr-aids-que-era-importado-dos-eua.shtml).

US\$879.65. However, if generic versions available in the international market or even the price set by Gilead in other countries are considered, it would be possible to obtain treatment costing between US\$204 patient/year to US\$85 patient/year.<sup>16</sup>

Although Gilead has signed voluntary licenses with Indian generic manufacturers restricting them to export to countries like Brazil, Cipla is an exception. The generic versions offered by this company would provide a cost per patient per year of US\$89; ten times cheaper than the price paid by Ministry of Health for the locally produced drug.

This price paid by the Ministry of Health could be justified by the strategic objective of developing the capacity of producing these essential medicines, which was also considered lower than the one paid to the originator company. However, questions about how prices for the local productions were defined remain open.

## **V. THE BRAZILIAN INTELLECTUAL PROPERTY SYSTEM**

Brazil has a long tradition in the area of intellectual property. It was the fourth country<sup>17</sup> in the world to establish protection of inventor's rights through the Charter of Prince Regent Dom João VI of 1809, during the colonial period of Brazil (Gama Cerqueira, 1946). Moreover, Brazil was one of the fourteen original signatories of the first international treaty on intellectual property – the Paris Convention (CUP – acronym in Portuguese)<sup>18</sup> of 1883. Brazil opted not to recognize patents for

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<sup>16</sup> Medecins Sans Frontières, *Untangling the Web of Antiretroviral Price Reductions*, (Geneva, July 2011). Available from <http://utw.msfaaccess.org/drugs/tenofovir-disoproxil-fumarate>.

<sup>17</sup> The first was England with the *Statute of Monopolies (1623)*; in second place, more than a century later, was the United States with the Constitution of 1787, which determined that the Congress would legislate on the protection of inventions (the first US law concerning patents was adopted in 1790); and third was France, which established privileges on invention in 1791 (Gama Cerqueira, 1946).

<sup>18</sup> This Convention underwent reforms in 1900 (Brussels), 1911 (Washington), 1925 (The Hague), 1934 (London), 1958 (Lisbon) and 1967 (Stockholm). The CUP allowed signatories to exclude from patentability any subject matter, according to their national interest.

pharmaceutical processes and products in its Industrial Property Code – CPI (Law 5772/1971, article 9, line c).

Brazil incorporated the World Trade Organization Trade Related Aspects of Intellectual Property Rights (TRIPS) through Decree 1,355 of 30 December 1994. In 1996, Brazil reformed its Industrial Property Law (Law 9.279/96) to put it in line with the minimum WTO standards. When establishing the new industrial property legislation, Brazil did not completely utilize the transition period allowed by TRIPS for developing countries to adapt their national legislation to the Agreement.

Intellectual property is protected by the Constitution of the Federal Republic of Brazil, but it is subordinate to Brazil's social interest and technological and economic development (Art 5, XXIX).

The following sections will provide an overview of the flexibilities available in Brazil to protect public health as allowed by the TRIPS Agreement, as well as some TRIPS-plus measures incorporated into the national legislation.

## **V.1 Flexibilities for the Protection of Public Health**

This section presents the flexibilities for the protection of public health adopted by the Brazilian industrial property legislation – Law 9.279/96. These flexibilities are mechanisms intended to mitigate the adverse effects of the rights conferred on patent holders, with a view to restoring the balance between intellectual property rights and the right of access to medicines.

As presented in table 4, Brazil incorporated compulsory licensing, the Bolar exception, the experimental use exception, and required ANVISA's prior consent for the grant of pharmaceutical patents.

Table 4

**TRIPS flexibilities for the protection of public health and their correspondent articles in the Brazilian Industrial Property Legislation**

<b>Flexibility</b>	<b>Definition</b>	<b>Article in the Brazilian Legislation</b>
Compulsory Licensing	<p>Provided for in Article 31 of the TRIPS Agreement</p> <p>The TRIPS Agreement allows compulsory licensing as part of the Agreement’s overall attempt to strike a balance between private and public interests. Nevertheless, the term “compulsory licensing” does not actually appear in the TRIPS Agreement. Instead, it uses the phrase “other uses without the authorization of the right holder”.</p>	<p>Articles 68-74 (Law 9.279/96)</p> <p>Decree 3.201/99 (regulates compulsory licenses for public interest purposes)</p>
Bolar exception	<p>Allowed by Article 30 of the TRIPS Agreement</p> <p>This exception allows manufacturers of generic medicines to obtain marketing approval prior to patent expiration, without the permission of the patent owner.</p>	<p>Item VII of Article 43, incorporated by Law 10196/2001</p>
Experimental use	<p>Allowed by Article 30 of the TRIPS Agreement</p> <p>This exception allows researchers to use patented inventions in their research, in order to understand the</p>	<p>Item II of Article 43</p>

<b>Flexibility</b>	<b>Definition</b>	<b>Article in the Brazilian Legislation</b>
	invention more fully. Reverse engineering depends upon experimental use.	
Health sector participation in examining pharmaceutical patent applications	Refers to the participation of the drug regulatory entity in the processes of examination of pharmaceutical patent applications.	Article 229c incorporated by Law 10196/2001
Parallel imports	<p>Allowed by Article 6 of the TRIPS Agreement</p> <p>When a product legally manufactured overseas is imported by another country without the consent of the owner of the intellectual property rights. The legal principle is “exhaustion”: once a patent holder has sold its product on the market, its patent rights are exhausted and he cannot prevent their resale to other countries. The TRIPS Agreement confirms that none of its provisions, with the exception of those dealing with non-discrimination, can be used to address the issue of exhaustion of intellectual property rights. The decision is left to domestic law.</p>	Article 68, paragraphs 3 & 4

Brazil has only once issued a compulsory license for the antiretroviral medicine Efavirenz in 2007 (detailed in box 1), on the grounds of public interest.

Parallel imports were incorporated into Brazilian law in a limited way, since their use is restricted to situations in which a compulsory license has been issued in cases of abuse of economic power (article 68, paragraphs 3&4, LPI) or national emergency or public interest (article 10, Decree 3.2101/99). A bill (Bill 139/99) was submitted to the National Congress to incorporate this flexibility in full (international exhaustion of rights).

Box 1

**Compulsory License of the antiretroviral Efavirenz**

Efavirenz is a patented medicine in Brazil, despite having been filed in other countries before the LPI (1992). This was possible because Brazil adopted a **pipeline** mechanism,<sup>19</sup> which allows patent protection to be granted retroactively.

During November 2006, the Brazilian government tried to negotiate with the patent-holder of Efavirenz – Merck Sharp & Dohme – for a price reduction, considering two important reasons:

- a) Merck Sharp & Dohme was selling Efavirenz at cheaper prices in countries at the same development level but with fewer people in need of treatment than Brazil;
- b) Indian generic versions were much cheaper, as cheap as US\$0.45/pill or an annual cost of US\$164.25/patient (Cipla, Ranbaxy and Aurobindo).

Merck, however, did not present an acceptable proposal to the Brazilian government, ignoring the national demand – which had been growing considerably each year. Furthermore, Merck disregarded Brazil's commitment to universal access and the fact that the current treatment protocol called for the use of Efavirenz

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<sup>19</sup> Its constitutionality was questioned before the Supreme Court by means of a 'Direct Action of Unconstitutionality'.

as one of the medicines for first-line treatment. Initially, the company presented a proposal to reduce the price by 2 per cent. After Efavirenz was declared an issue of public interest, Merck reduced the price by 30 per cent.

The government considered Merck's proposal unsatisfactory and finally, in May 2007, issued a compulsory license for the initial import of generic versions produced in India and, thereafter, for locally manufactured generics. The generic version of the medicine was then imported from India at a cost of R\$365 per patient/year,<sup>20</sup> a third of the price offered by Merck.

Brazil produced its first batch of Efavirenz in January 2009 at the official pharmaceutical laboratory of the Oswaldo Cruz Foundation, the Institute of Technology in Drugs, Farmanguinhos, for only R\$1.35/pill, 45 per cent of the price set by Merck before the compulsory license (Estado de São Paulo, 2009).

The participation of the health sector in examining pharmaceutical patent applications was implemented by the "Provisional Measure"<sup>21</sup> 2.006/99, which evolved into Law 10.296/2001 that included article 229c in the LPI. This mechanism determined that patents in the pharmaceutical field could only be granted with the prior consent of the Brazilian National Sanitary Surveillance Agency (ANVISA), the government body responsible for sanitary safety and quality assurance of pharmaceutical drugs in the country. The legislation was justified (as explained in the presentation of the motives of the "Provisional Measure" 2.006/99) on the grounds that "the work between the National Institute of Industrial Property – INPI and ANVISA would guarantee the best procedure for pharmaceutical patents, comparable to the most advanced systems of patent control and sanitary surveillance in function in developed countries." Box 2 presents some published data

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<sup>20</sup> The paid value for a tablet for adult use (600 mg) was R\$1. Each adult used one tablet per day, totalling a cost of R\$365 per patient/year or US\$190 per patient/year (considering the official exchange rate of R\$1.91 at the time the shipment was received). Radiobrás, 2007.

<sup>21</sup> The provisional mechanism established by article 62 of the Brazilian Constitution states that in important and urgent cases, the President of the Republic may adopt provisional measures that must subsequently be submitted to the National Congress.

related to the work developed by ANVISA within the scope of the prior consent mechanism.

The prior consent mechanism of ANVISA has been criticized by the INPI and by patent holders through judicial<sup>22</sup> and administrative actions, as well as through legislative bills,<sup>23</sup> which seek to eliminate or weaken its power.

In 2007 INPI requested that the Brazilian Attorney General (AGU – acronym in Portuguese), responsible for managing conflicts between State bodies, review the alleged conflict of duties between the INPI and ANVISA. The first legal opinion presented by the AGU was issued in 2009.<sup>24</sup> Its main conclusion was to restrict ANVISA's role to the analysis of potential harmful effects to human health of the product claimed in the patent application. In other words, ANVISA would not be competent to analyse the fulfilment of the patentability requirements of novelty, industrial application and inventiveness.

The analysis of adverse effects of a product is requested when a company presents data before the Drug Regulatory Authority (DRA) to obtain market approval. This kind of information is normally not submitted with pharmaceutical patent applications; hence, if AGU's opinion were followed, ANVISA would have no effective role in patent examination. Some might argue that data on safety of a medicine could be presented in a patent application in cases of compounds or new uses and indications – which might be true. However, these types of

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<sup>22</sup> One judicial action is lawsuit No. 2004.51.01.506840-0 currently pending before the 37th Federal Court of Rio de Janeiro. The pharmaceutical company Roche requested the grant of a patent for the hydrochloride product of valganciclovir, principal active ingredient of the medicine Valcyte®, which is used by patients with AIDS. The grant of the patent was not consented by ANVISA. The company alleged that the participation of ANVISA in the patent examination was illegal and was contrary to the TRIPS Agreement and that, in the case that the participation of ANVISA were legitimate, it would have gone beyond its competence in analyzing the patentability requirements.

<sup>23</sup> Bill 3.709/2008, proposed by Deputy Rafael Guerra (PSDB-MG), intends to limit the prior consent to pipeline patents, which in practice would mean the elimination of ANVISA's role, since shortly there will be no pipeline patent applications to be examined.

<sup>24</sup> AGU. Parecer 210/PGF/AE/2009. Annex 2 (in Portuguese).



applications do not reflect the universe of patents filed in the pharmaceuticals field, which overwhelmingly refer to incremental innovation According to the legal opinion of the AGU on Prior Consent:

“[ANVISA] will not be able to re-examine the patentability requirement, except in cases of new drugs or new ‘discovered products’ for the use of drugs that are already patented and could – even if only potentially – cause adverse outcomes to the health of the population, especially in the case that the efficiency is dubious, such as when the determined medicine does not produce the hoped-for therapeutic effect, which could result in compromising healthcare. In such situations, it is recommended that ANVISA protests against the granting of a patent”.

The analysis of harmful effects to health of a product claimed in a patent application goes beyond the three patentability requirements of novelty, inventiveness and industrial application required by TRIPS, and could be considered a fourth patentability requirement. In this case, this fourth requirement would be infringing the TRIPS Agreement.

Although many stakeholders reacted to the AGU legal opinion – such as ANVISA, public health civil society groups (GTPI/Rebrip),<sup>25</sup> the Ministry of Science and Technology<sup>26</sup> and others – requesting its review, on 7 January 2011, the AGU published a final opinion supporting the previous one and adding that ANVISA could present arguments to support the analysis (oppositions) made by INPI. As it is a final opinion, it is supposed to be adopted by INPI and ANVISA.<sup>27</sup>

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<sup>25</sup> Letter to Federal General-Prosecutor Marcelo Siqueira for the maintenance of ANVISA’s prior consent. Available from <http://www.petitiononline.com/gtpi2/petition.html>.

<sup>26</sup> Information available at ESTADO DE SÃO PAULO. Ministries of Health and Science and Technology intervene for ANVISA in the case of patents. [http://www.estadao.com.br/estadaodehoje/20100812/not\\_imp593908,0.php](http://www.estadao.com.br/estadaodehoje/20100812/not_imp593908,0.php).

<sup>27</sup> AGU. Processo n. 00407.005325/2007-71. Available (in Portuguese) from: [http://www.agu.gov.br/sistemas/site/TemplateImagemTextoThumb.aspx?idConteudo=153676&id\\_site=3](http://www.agu.gov.br/sistemas/site/TemplateImagemTextoThumb.aspx?idConteudo=153676&id_site=3).

On 3 February 2011, public health civil society groups, mostly non-governmental organization members of the Working Group on Intellectual Property from the Brazilian Network for the Integration of Peoples (GTPI/Rebrip), made a submission to the UN Special Rapporteur on the Right of Everyone to the Enjoyment of the Highest Attainable Standard of Physical and Mental Health arguing that the AGU legal opinion was weakening a public health flexibility allowed by the TRIPS Agreement.<sup>28</sup>

**Box 2**

**Some data on ANVISA's prior consent**

For the analysis of pharmaceutical patent applications, ANVISA created the Coordination of Intellectual Property (COOPI). According to a technical note published by COOPI,<sup>29</sup> from 2001 to 2009, ANVISA analysed 1,346 patent applications, out of which 988 were given prior consent, 119 were not given prior consent, 90 were denied by INPI after ANVISA's participation in the process and 149 are pending (awaiting ANVISA's analysis or awaiting the applicant's response to requests made by the agency).

The reasons for ANVISA not giving prior consent to 119 applications are as follows: 47.9 per cent due to lack of novelty; 22.7 per cent due to lack of inventiveness; 16 per cent due to insufficient disclosure; 5.9 per cent were products of nature; 5 per cent were undefined objects; 1.7 per cent were due to late modifications on the application and 0.8 per cent were applications filed outside the time limit. It is important to note that applications which were presented to ANVISA for analysis had been previously considered by INPI as patentable. Although ANVISA denied those 119 applications, 106 of them were not published by INPI, which means that they are still pending.

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<sup>28</sup> For the complete text of the complaint, go to: <http://www.patentes.org.br/media/file/Urgent%20appeal%20against%20Brazil%20-%20by%20GTPI%20%28with%20annexes%29.pdf>.

<sup>29</sup> Annex 1 of the document available from: <http://www.patentes.org.br/media/file/Urgent%20appeal%20against%20Brazil%20-%20by%20GTPI%20%28with%20annexes%29.pdf>.

It is worth mentioning that although 998 applications received ANVISA's prior consent, only 40 per cent got its final approval after changes were requested by the agency. These changes meant in several cases the reduction of the scope of claims - due to lack of novelty, inventiveness or for non-patentable subject matter. So ANVISA's role is not only about providing a restrictive analysis, from a public health perspective, but also about enhancing the quality of patent examination and avoiding the evergreening of patents.

This is also reflected in the 90 cases in which INPI changed its position after ANVISA's participation in the analyses. In other words, those applications were initially patentable by INPI, but after ANVISA's view, INPI changed its position.

Another important tool to enhance the quality of patent examination and to avoid the evergreening of patents is patent opposition. In Brazil, pre-grant opposition is provided for in the industrial property legislation in a very limited manner as a "support to examination".

According to article 31 of Law 9.279/96, interested parties are allowed to present documents and information to assist in the examination of patent applications until the end of the examination by the Brazilian Patent Office. The interested parties that submit information do not participate in the formal process and the applicant is not notified of their filing. The patent examiners then consider the relevance of the data and accept or refuse it in their review. This arrangement distinguishes itself from the pre-grant opposition system provided for in the former patent legislation, which gave a deadline of 90 days after the examination to file a pre-grant opposition. Also, the application of the pre-grant opposition was notified to the applicant who could rebut the arguments.

Box 3 presents the Tenofovir case in which the patent application was contested by Farmanguinhos and civil society groups.

Box 3

**Contesting Tenofovir (TDF) patent application**

In December 2005, Farmanguinhos (Fiocruz) presented an opposition contesting the patent application related to the salt form of the anti-AIDS medicine tenofovir. In December 2006, the Brazilian Interdisciplinary AIDS Association (ABIA) and other organizations<sup>30</sup> also presented arguments before INPI to contest the granting of this patent. In 2007, Fiocruz filed an additional opposition.

According to data from the Departments of STDs and AIDS of the Ministry of Health, in 2007 Brazil spent more than R\$89 million towards the procurement of TDF, representing 14.94 per cent of the budget for the purchase of ARVs in Brazil that year. TDF was the second most expensive medicine for the treatment programme of HIV/AIDS in Brazil, after Atazanavir (Reyataz® from Bristol-Myers Squibb), which accounted for 22.38 per cent of the resources destined for the procurement of ARVs in the same year. For this reason, in April 2008, the Ministry of Health declared TDF of public interest for purpose of priority examination of the patent application.

The oppositions called for the dismissal of the patent application for TDF in Brazil, based on the argument of lack of inventiveness. Several organizations and the public laboratory alleged that there was not a sufficient inventive step that justified patent protection, since the achievement of the compound (TDF is in reality a salt of tenofovir) is trivial for a technician.

On 30 June 2009, INPI rejected the patent application for TDF because the compound, the composition and the asserted claims

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<sup>30</sup> The organizations that submitted the petition work together in the Working Group of Intellectual Property of REBRIP, among which are: Conectas Direitos Humanos; Grupo pela Valorização, Integração, e Dignidade do Doente de AIDS de São Paulo – PELA VIDDA-SP; Grupo de Apoio à Prevenção à AIDS – GAPA SP; Grupo de Apoio à Prevenção da AIDS do Rio Grande do Sul – GAPA/RS; Gestos Soropositividade Comunicação e Gênero and Grupo de Incentivo à Vida – GIV.

were not considered inventive, not complying with articles 8 and 13 of LPI.

Although the patent application for TDF, as mentioned above, had been rejected, on 31 March 2009, the INPI accepted a divisional patent application of TDF (PI9816239-0), which had been filed on 10 July 2008 by the patent applicant (approximately three months before the first dismissal).

In November 2009, Brazilian civil society organizations submitted documents<sup>31</sup> opposing the divisional application made by Gilead based on arguments that the company included new claims which did not exist in the original application, and that those claims were related to use. It was emphasized that although the possibility of voluntary divisional patent applications are allowed by Brazilian law and the divisional patent application has the same lifespan of the original patent, it had been employed in this case as a strategy to unduly prolong the patent protection or to create legal uncertainty.

Gilead also went to Court in an attempt to reverse the INPI decision to reject the original application.

Although both decisions – in the Court and the divisional application – are pending, the Brazilian government decided to move forward with local production based on public-private partnerships involving NORTEC and FUNED.

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<sup>31</sup> The organizations that submitted the petition work together in the Working Group of Intellectual Property of REBRIP. They include: Associação Brasileira Interdisciplinar de AIDS – ABIA; Conectas Direitos Humanos; Grupo pela Valorização, Integração, e Dignidade do Doente de AIDS de São Paulo – PELA VIDDÁ-SP; Grupo de Apoio à Prevenção à AIDS – GAPA SP; Grupo de Apoio à Prevenção da AIDS do Rio Grande do Sul – GAPA/RS; Gestos Soropositividade Comunicação e Gênero and Grupo de Incentivo à Vida – GIV; Instituto Brasileiro de Defesa do Consumidor – IDEC; Federação Nacional dos Farmacêuticos – FENAFAR; Rede Nacional de Pessoas Vivendo com HIV/AIDS Núcleo São Luiz – RNP+/SLS.

## **V.2 TRIPS-plus Provisions Adopted in the Brazilian Industrial Property Legislation**

TRIPS-plus provisions are those beyond the minimum standards demanded by the TRIPS Agreement. Some of them may affect access to medicines. In the Brazilian legal system, a TRIPS-plus provision related to pharmaceuticals has been the “pipeline” mechanism.<sup>32</sup>

The pipeline mechanism was established in articles 230 and 231 of the LPI – which allowed for patent filings in technological areas for which Brazil had not yet granted patents – principally medicines and food. It is one of the most controversial measures under the new LPI.

The pipeline patents were granted under a different process and mechanism than other patents filed in Brazil. The filing of a patent application based on the pipeline mechanism was accepted in the year, between May 1996 and May 1997. It allowed revalidating patents of medicines, food and chemical/pharmaceutical products and processes granted in other countries. As these patents had already been filed in other countries, the information on the respective inventions had already been published in magazines of industrial property and other media. Therefore, when such applications were filed in Brazil, they did not fulfil the requirement of novelty because the information had already been in the public domain (Miranda, Silva, and Pereira, 2009).

The Brazilian Prosecutor General, in addressing a petition presented by the Brazilian Network of Integrated Peoples (REBRIP) and by the National Federation of Pharmacists in November 2007, filed a Direct Action of Unconstitutionality (ADI/4234) calling for the declaration of unconstitutionality of articles 230 and 231 of the LPI which established the pipeline mechanism (Reis *et al.*, 2009; Vieira *et al.*, 2010). Up to the time of writing this chapter, a date is yet to be set for the hearing of the ADI by the Supreme Court (STF).

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<sup>32</sup> For further information on other bills submitted to the National Congress, see Renata Reis, Veriano Tertto Jr. and Maria Cristina Pimenta (Organizers), *Intellectual Property Rights and Access to ARV Medicines: Civil Society Resistance in the Global South* (Rio de Janeiro, ABIA, 2009). Available from <http://www.patentes.org.br/media/file/Publica%C3%A7%C3%B5es/Intelectual%20Property.pdf>.

The aforementioned ADI asserts that pipeline patents violate the Federal Constitution because they grant patent protection retroactively for knowledge that had already been in the public domain, violating the principle of non-derogation from the public domain and the principle of absolute novelty (article 11, paragraph 1 of the LPI). Furthermore, they do not fulfil the conditions that justify, under the Constitution, the protection of intellectual property, insofar as they do not assist the economic, technological and social interest of the country.

The declaration of unconstitutionality could put back in the public domain hundreds<sup>33</sup> of essential medicines that had been unduly monopolized.<sup>34</sup>

Box 4 presents two strategies adopted by public health civil society groups to overcome high prices set by Abbott for the anti-AIDS medicine lopinavir/ritonavir, which was protected through the pipeline mechanism.

**Box 4**

**Patent of ARV Kaletra® (lopinavir/ritonavir) PI1100397-9 – filed on 30 April 1997**

In 2005, during price negotiations with Abbot for lopinavir/ritonavir (Kaletra®) – which was being used by 17,000 people at the time – the Brazilian government made the first step toward the issuance of a compulsory license by declaring, via an official decree, that the medicine was of public interest. After months of negotiations, the Ministry of Health made an agreement with Abbott accepting the fixed price of US\$1,380 per patient/year until 2011, disregarding the potential incremental demand of the drug and international variation of prices. In addition, the agreement also stipulated the guarantee that a compulsory license would not be issued for lopinavir/ritonavir.

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<sup>33</sup> Non-exhaustive list of protected medicines by pipeline patents available from [http://www.abiaids.org.br/\\_img/media/ID\\_pipeline.xls](http://www.abiaids.org.br/_img/media/ID_pipeline.xls).

<sup>34</sup> For more information, Veriano Terto Jr., Maria Cristina Pimenta and Renata Reis (Organizers), *Questions & Answers about Pipeline Patents: How do they Affect your Health* (Rio de Janeiro, ABIA, 2009). Available from [http://www.abiaids.org.br/\\_img/media/QuestAnswers\\_PIPELINE\\_INGLES.pdf](http://www.abiaids.org.br/_img/media/QuestAnswers_PIPELINE_INGLES.pdf).

Once the agreement was signed, Brazilian civil society organizations (GTPI/REBRIP), in conjunction with the Federal prosecutor's office, filed an unprecedented civil public action<sup>35</sup> against the government and Abbott demanding that a compulsory license be issued for lopinavir/ritonavir. However, the request was denied on the argument that the issuance of a compulsory license would generate retaliations from developed countries, the possible shortage of the medicine and the absence of national production. In 2009 other organizations and movements in Colombia also filed a civil public action demanding the compulsory license of lopinavir/ritonavir in their country. In 2010, a final decision denied the request of compulsory license made by civil society.

Furthermore, in June 1999, Abbott filed a divisional patent application (PI1101190-4) of the original patent for lopinavir/ritonavir at the INPI. In 2006, non-governmental organizations from GTPI/REBRIP submitted documents for an opposition to this divisional patent application, arguing that there was no legal basis for divisional patent applications for pipeline patents. The patent was rejected by INPI.

## **VI. TRENDS IN THE GRANTING OF PHARMACEUTICAL PATENTS IN BRAZIL, 2003-2008**

### **VI.1 Introduction and Objective**

The study aimed to evaluate, both in quantitative and qualitative terms, pharmaceutical patents granted in Brazil between 2003 and 2008. Among patents identified, those related to antiretrovirals (HIV/AIDS) and to cancer medicines were selected. The collection of empirical data also allowed the identification of gaps in the current patent system in Brazil. Finally, patent applications made by national pharmaceutical manufacturers were investigated, followed by a brief discussion about

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<sup>35</sup> Lawsuit 2005.34.00.035604-3, 15th Civil Court of the Federal Justice of the Judiciary Section of the Federal District.



the potential benefits and constraints of the patent system as a way to stimulate innovation in the pharmaceutical field in Brazil.

The objective of this section is to analyse trends in the granting of pharmaceutical patents and potential implications on generic competition and access to medicines in Brazil.

## **VI.2 Methodology – Patent Search and Qualitative Selection**

The period 2003-2008 was defined to collect pharmaceutical patents granted in Brazil. The following steps were adopted to achieve this:

- The National Institute of Industrial Property – INPI (Brazilian patent office) has a Centre of Information (CEDIN<sup>36</sup>) to provide information on patents granted on specific subject matters. In the current study, the information requested covered: (a) patents granted between 2003 and 2008, (b) patents granted under the classification C07, C08, A61K, B82B, and C12P.
- Once the information on granted patents was provided by CEDIN, the patent documents were downloaded from the INPI patent database ([www.inpi.gov.br](http://www.inpi.gov.br)) and those which did not have a national version, were obtained from the Espacenet. Some patents were not available in any of the two options (national or international version) or were impossible to download (document too large). In both cases, they were considered as losses. Those that did not have a national version, but did have an English version, were included for analysis.
- There was a need for further analysis and selection of pharmaceutical patents to be included in the database. Criteria of inclusion:
  - Type of order: two kinds of orders were considered – 9.1<sup>37</sup> (publication that the patent was granted) and

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<sup>36</sup> Centro de Disseminação da Informação Tecnológica.

<sup>37</sup> Deferimento (Portuguese term). Source: [www.inpi.gov.br](http://www.inpi.gov.br).

16.1<sup>38</sup> (expedition of the patent). Some patents obtained the order 16.1 in 2009, but were granted (9.1) in 2008. In these cases, they were included.

- Limitations of the study: due to the high cost to obtain the filed patent with the final claims (after examination), it was decided to work with information available on the INPI webpage and also Espacenet. However, most of the documents downloaded included the KIND A code which means that the claims were those filed, but not the final claims. Only when there are KIND B, B1 and B2 codes does this indicate the inclusion of final claims. It is known that many times the claims are changed after examination.

The second step of patent selection was a qualitative analysis in order to identify the pharmaceutical patents. This included reading the title, abstract and, when necessary, the claims. Patents were excluded from the database when they:

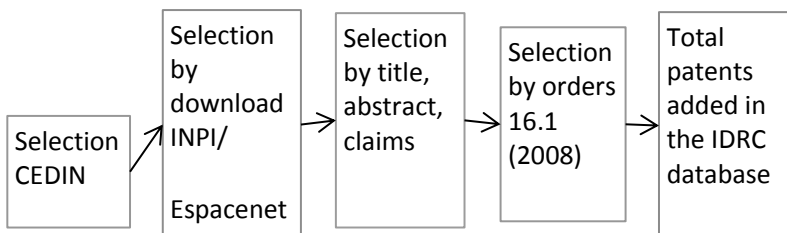
- Were identified as herbicides, pesticides, chemical processes not linked to pharmaceuticals, cosmetics and hygiene (dental products), fungicides with no human specification, veterinary products, formulation without any pharmaceutical link (API etc.);
- Had the order 11.4, which means filed. This means that they were granted (9.1), but did not achieve the order 16.1 due to lack of payment. The decision was made not to include these patents in the database, but to consider them when discussing the use of the patent system for the purpose of creating legal uncertainty.

Patents which had order 24.3, which means “restoration”, were included in the database. Restoration means that the patent owner did not pay the annual fee (sometimes more than once) to keep the patent in force. In this case, the patents were included in the database.

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<sup>38</sup> Concessão de patente ou certificado de adição de invenção (Portuguese term). Source: [www.inpi.gov.br](http://www.inpi.gov.br).

One patent received order 21.6 (extinction) and was included in the database. The following scheme summarizes the steps taken for patent selection for the database:



### VI.3 Selection of HIV/AIDS and Cancer Patents

The selection of HIV/AIDS patents (antiretrovirals – ARVs) was made by reading abstracts and claims, considering key-words such as “HIV”, “AIDS”, “virus da imunodeficiencia adquirida humana”. In order to ensure that no ARVs protected in the period established for the study were missed, the findings were compared to the ARV patent landscape study being conducted by ABIA.<sup>39</sup>

In relation to cancer, the first step was to select all patents which included in the abstract key-words such as “tumour”, “cancer” and “antineoplásico” and “neoplasia”. In order to identify whether those patents were linked to cancer medicines available in the market, the US patent number was identified in Espacenet and, with this number, the corresponding medicine was searched for in the FDA Orange Book.<sup>40</sup>

### VI.4 Legal Cases

The methodology adopted to identify those patents that were under lawsuits was based on the publication of order 22.15, which means

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<sup>39</sup> “Panorama do Status de Patentes e Registro Sanitário dos Medicamentos Antiretrovirais no Brasil” – Ministério da Saúde – Secretaria de Vigilância em Saúde – Departamento Nacional de DST, AIDS e Hepatites Virais e UNESCO.

<sup>40</sup> <http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm>.

“sub judice” or notification that there is a lawsuit related to the patent. This information was collected from the INPI patent database.<sup>41</sup>

## **VI.5 Patenting by Brazilian Pharmaceutical Manufacturers**

Brazilian pharmaceutical manufacturers (public and private) are organized in several Associations – Abifina, Abiquif, Alfob, Abiquim, Pro-Genericos, Alanac. For the purposes of this research, it was decided to investigate patenting trends of manufacturers that are members of the Brazilian Association of Fine Chemistry (Abifina). Abifina “is composed of companies that work in the industrial complex of fine chemistry. It does not discriminate against companies by origin of capital, but requests that they are committed to manufacturing and innovation in Brazil. Currently, most of the companies related to the pharmaceutical field are national private or public laboratories.” Abifina includes the following areas of fine chemistry: agrochemicals, pharmaceuticals, medicines, vaccines for human and veterinary use, catalysers and additives, dyes and organic pigments, and intermediates for synthesis.<sup>42</sup>

Patent applications of manufacturers<sup>43</sup> linked to the pharmaceutical sector were downloaded from the INPI website ([www.inpi.gov.br](http://www.inpi.gov.br)) by company name.

It is important to mention that through this research a patent granted to a public manufacturer (Fiocruz) was found which was not included in the information provided by CEDIN, but was within the scope of the study, and hence, included therein.

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<sup>41</sup><http://pesquisa.inpi.gov.br/MarcaPatente/jsp/servimg/servimg.jsp?BasePesquisa=P atentes>.

<sup>42</sup> Available from [www.abifina.org.br](http://www.abifina.org.br).

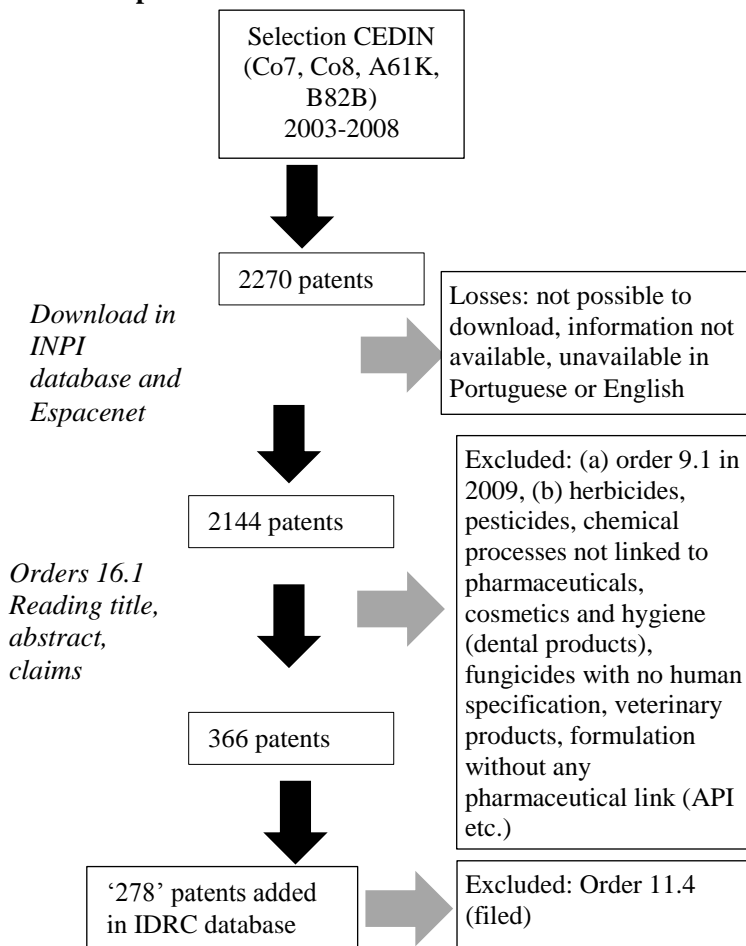
<sup>43</sup> Selected manufacturers working in the pharmaceutical field: Aché, Alfa Rio Química, Biomanguinhos (Fiocruz), EMS, Globe Química, Instituto Vital Brazil, Lab Simões, Nortec, Núcleo de Pesquisa Aplicada, Nurfam, Cristália, Biolab, Geolab, Laborvida, Medapi, Cyg, Hebron, Eurofarma, Libbs, Farmanguinhos (Fiocruz), Quiral, Microbiológica, União Química Farmacêutica.

## VII. RESULTS AND DISCUSSION

### VII.1 Patent Search and Quality of the Brazilian Patent System

A total number of 278 pharmaceutical patents were identified for the period 2003-2008. The flow chart below summarizes the results per stage of patent selection.

#### Flow-chart of patent selection

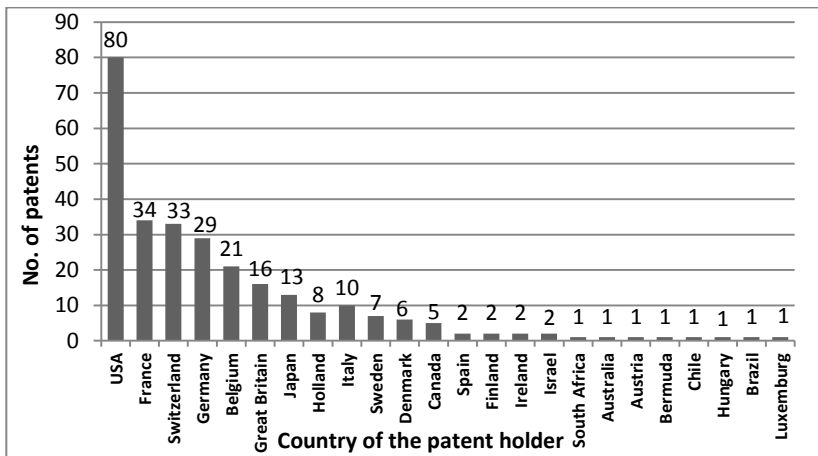


When analyzing patents according to country of origin of the patent holder, only one patent found belonged to a Brazilian manufacturer (see figure 6). Twenty-nine per cent of the patents were filled by applicants from the United States of America (USA), and five countries in total (USA, France, Switzerland, Germany and Belgium) accounted for 71 per cent of the pharmaceutical patents granted in Brazil between 2003 and 2008.

These findings correlate with previous studies which analysed patents filed (not granted) in Brazil in the pharmaceutical sector between 1992 and 2002 (Bermudez *et al*, 2000; Oliveira *et al*, 2004), with a focus on pharmaceutical products. One of the results Bermudez *et al.* found was that between 1992 and 2002, 85 per cent of the applications were made by applicants from the USA (41 per cent), Germany (21.4 per cent), France (9.1 per cent), Great Britain (7.7 per cent) and Switzerland (5.9 per cent).

The previous studies also showed that between 1992 and 1995, Brazilian applicants did not account for any of the applications, while from 1996-2002 this scenario changed to 3.1 per cent of the total number of applications.

Figure 6  
**Distribution of patents granted in the pharmaceutical sector by country of origin of patent holder, 2003-2008**



It is important to note that 70 per cent (194) of the patents granted were filed before 1997, when the Brazilian Industrial Property Law (Law 9.279/96) became operative for the grant of patent protection for pharmaceuticals, and 44 per cent of them were applications made before 1995.

Law 9.279/96 included the so-called “pipeline” mechanism (discussed in detail in the previous section). Pipeline patents (or revalidation patents) are regulated by articles 230 and 231. These articles allow patent applications for technological fields that Brazil did not recognize during the previous legislation (primarily medicines and foods). It has always been a controversial mechanism, even during the formulation of the new Brazilian Industrial Property Law.

Pipeline patent applications went through a process of approval different from other patent applications in Brazil. The filing of such applications was accepted only during a period of one year, from May 1996 to May 1997, and INPI “revalidated” them when the corresponding patents were protected in the country of origin. They were not subjected to evaluation under the patentability requirements – novelty, inventiveness and industrial application.

However, the patents found in the present study were not obtained under this mechanism, but in compliance with article 229, incorporated into the legislation through an amendment made in 2001 – Law 10.916/01:

“229. The provisions of this Law shall be applied to all pending applications, except with respect to the patentability of applications filed up until December 31, 1994, whose object of protection comprises substances, matter or products obtained by chemical means or processes and alimentary and chemical-pharmaceutical substances, matter, blends or products and medications of any type, as well as the respective attainment or modification processes, and whose applicants have not used the right provided in Articles 230 and 231 of this Law, which shall be considered rejected for all purposes, the Brazilian

Patent and Trademark Office being bound to publish the referred rejections.

Sole Paragraph. The criteria for patentability set in this Law shall be applied to applications pertaining to pharmaceutical and chemical products intended for agriculture, which were filed between January 1, 1995 and May 14, 1997, on the effective filing date of the application in Brazil or of the priority, wherever applicable, the protection being assured from the date when patent is granted, through the remaining term counted from the filing date in Brazil, limited to the term provided in the caput of Article 40.<sup>44</sup>

So, in concrete terms, Brazil did not make any use of the transition period allowed by TRIPS and even went further, by accepting applications first filed even before the entry into force of the obligations under the TRIPS Agreement.

When the selected patents were matched with ANVISA's database, it was found that 6 per cent were granted by INPI without being analysed by ANVISA in accordance with the "prior consent" mechanism. This reflects non-compliance with Law 9.279/96 (article 229-c) and raises concerns on whether all pharmaceutical applications are really going through analysis by both bodies.

As presented in figure 7, the backlog (time between the filing of the application and the granting of the patent) for patents granted from 2003 to 2008 was nine years for 22.6 per cent of the cases and from 8 to 12 years in 70 per cent of the cases. In relation to the companies that obtained most pharmaceutical patents in Brazil, 26.6 per cent of the total analysed was obtained by six companies as described in figure 8.

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<sup>44</sup> English version of Brazilian Industrial Property law – Law 9.279/96, amendment Law 10.196/01. Source: World Intellectual Property Organization, Collection of Law for Electronic Access: [http://www.wipo.int/wipolex/en/text.jsp?file\\_id=125409](http://www.wipo.int/wipolex/en/text.jsp?file_id=125409).



Figure 7

**Backlog of pharmaceutical patents granted in Brazil, 2003-2008**

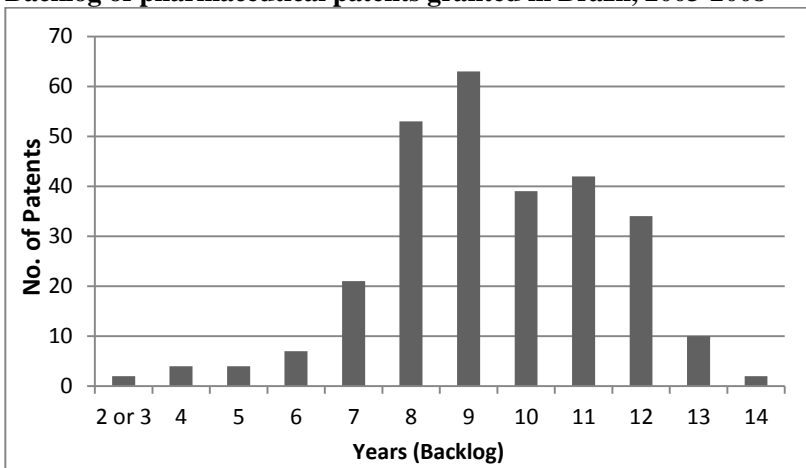
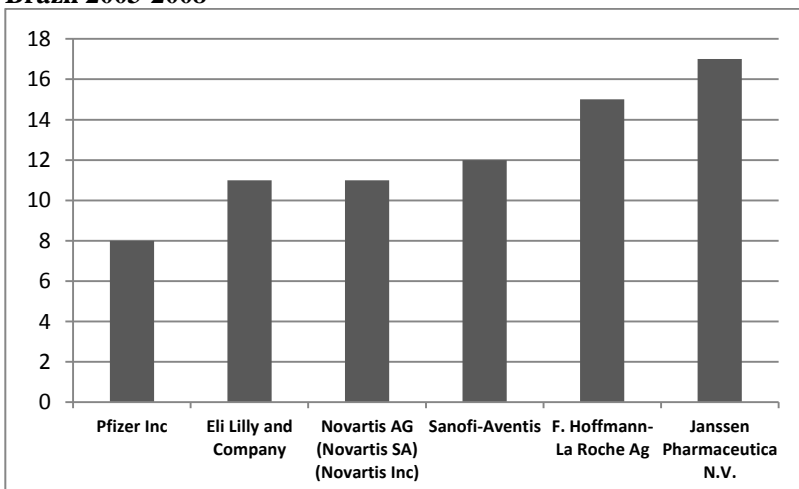


Figure 8

**Patents granted in the pharmaceutical sector by filing company, Brazil 2003-2008**



Findings related to the lack of payment of annual fees (order 24.3) deliver important inputs for the discussion on the operation of the

Brazilian patent office. Annual fees and the possibility of restoration are established by articles 84-87 of the Brazilian legislation.<sup>45</sup> Although the patent holder has the right to request “restoration”, it is necessary to pay annual fees to maintain the patent in force. However, as found in the present study, some patent holders went six years without the payment of an annual fee, without INPI imposing any of the penalties established by law.

According to what was found in the INPI patent database, there were patents with unpaid annual fees ranging from one to six years, without any action determining the filing status of the process or extinction of the patent (see figure 9).

It is not possible to infer the reason for patent holders not paying annual fees, as well as the reasons for INPI not filing or extinguishing those unpaid patents, despite the provisions established by the law. Two hypotheses were raised, but would need further investigation:

- These patents do not cover any strategic medicine in the market, not being a priority patent to protect the technology, but rather a secondary patent;

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<sup>45</sup> According to the Industrial Property Code (Law 9.279/96):

“CHAPTER XII – ANNUAL FEE

84. The applicant and the patent holder are subject to the payment of an annual fee three years after the filing date.

(1) Anticipated payment of the annual fee shall be regulated by INPI.

(2) Payment shall be made within the first 3 (three) months of each annual period, but it may also be made within the following 6 (six) months, independently of any notification, upon payment of an additional fee.

85. The provisions of the previous Article apply to international applications filed under a treaty in force in Brazil, and the payment of the annual fees that fell due prior to the date of entry into the national processing shall be made within a period of 3 (three) months of that date.

86. The failure to pay the annual fee, in accordance with provisions of Articles 84 and 85, shall result in the dismissal of the application or extinguishment of the patent.

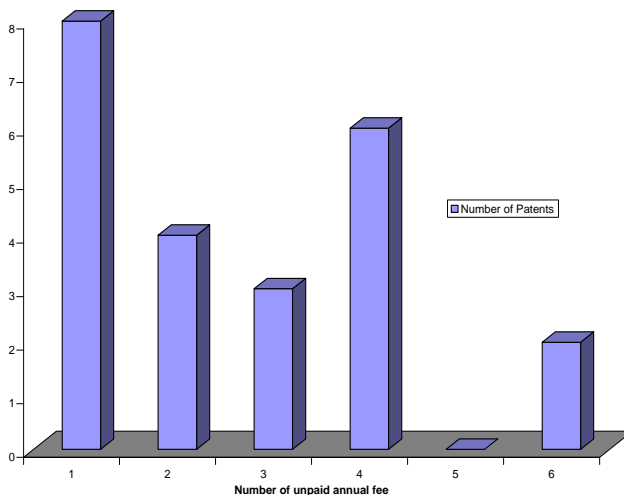
CHAPTER XIII – RESTORATION

87. The patent application or the patent may be restored, if the applicant or titleholder so requests, within 3 (three) months from the notification of the dismissal of the application or the lapsing of the patent, upon payment of a specific fee.”

- Patent holders are taking advantage of the lack of enforcement of penalties by INPI and creating legal uncertainty.

Figure 9

**Number of patents according to number of unpaid annual fees, 2003-2008**



In relation to patents under lawsuits, only two were found, as shown in table 5. The authors tried to obtain more information for a deeper analysis, but both were unavailable to the public at the time of the research.

Table 5

**Patents under lawsuit found in the INPI patent database**

Patent	Action Number	Local	Petitioner	Defendant
BR950925 7-9	No. 2006.51.015 37648-5	16 <sup>a</sup> Vara Federal Rio de Janeiro	Cephalon INC	INPI

<b>Patent</b>	<b>Action Number</b>	<b>Local</b>	<b>Petitioner</b>	<b>Defendant</b>
	No. 2006.34.00.0 36923-5  No. 2008.51.01.8 14865-4 PS: attached is the number of appeal	35 <sup>a</sup> Vara Federal Previdenciária Rio de Janeiro		
BR980699 6-9	No: 2009.51.01.8 05669-7	35 <sup>a</sup> Vara Federal Previdenciária do Rio de Janeiro	Cristalia Produtos Quimicos Farmaceuticos LTDA	INPI and Central Glass Company and Abbott Laboratories

## **VII.2 Reflections on Transparency of the Patent System in Brazil**

Based on the current empirical study, it is possible to make some reflections related to the challenges on accessing accurate information on patents. Some of those challenges are linked to the findings and problems observed in the way the Brazilian patent office is working and others are structural, related to the system of filing and granting of patents. Some of the problems identified related to INPI are the following:

- a) There were missing patents provided by CEDIN according to established classification, which were found during the research (two cases) through other ways. For this reason, it is not possible to know the reasons for such a gap, which brings uncertainty about patent coverage;
- b) The analysis of the content – specifications and approved scope of claims – was limited because the documents available on the INPI website did not include the content after analysis by INPI and ANVISA. It was impossible,

through the webpage, to identify the final scope of claims of patented inventions. This is a key issue for the evaluation of the quality of examination and correlates to a recent study developed by Silva (2008) which evaluated reviews made by ANVISA within its mandate of granting “prior consent”. In this study, Silva evaluated 770 reviews from ANVISA between June 2001 and December 2006. Findings have shown that only 3.4 per cent were not approved by ANVISA. However, from a group of 232 applications examined by ANVISA, 34 per cent were considered as lacking sufficient disclosure, which in many cases supported a limitation to the scope of claims.

- c) Due to lack of information on the INPI website regarding the final claims of key patents related to HIV medicines, the second option was to get hard copies from the patent office. However, as there were less than three months remaining to conclude the project, and based on other reports and previous experience showing that it takes time for INPI to provide this information, it was not possible to obtain it.
- d) A structural problem also found when conducting the current study, is the difficulty to identify patents related to specific medicines. This is a complex task, and in many cases, an unfeasible one. This might be easier if it were possible to access paid databases. But finding patented medicines using information available to the public requires time-consuming searches of several databases – such as the FDA Orange Book or the Food and Health Canada Patent Register (Amin, 2010). Even this method does not guarantee that patent families will be found. This suggests a structural problem of lack of transparency of the patent system.

### **VII.3 Patents Related to HIV/AIDS and Cancer**

In 2010, the Brazilian Department of STD/AIDS and Viral Hepatitis of the Ministry of Health published a document entitled “Universal Access in Brazil: current scenario, achievements, challenges and

perspectives".<sup>46</sup> This document provides an overview of which ARVs are locally produced and which ones are imported as a consequence of a monopolistic situation.

Table 6  
**ARV Patents Granted, 2003-2008**

<b>Patent number</b>	<b>ARV</b>	<b>Type</b>	<b>Patent holder</b>
PI9506977-1	Key-intermediates for synthesis of protease inhibitor	Chemical	Merck
PI9808060-1	Lamivudine	Formulation	Glaxo Group Limited
PI9815861-9*(WO9961002)	Didanosine	Formulation (enteric coated pharmaceutical composition and method of manufacturing)	Bristol Myers Squibb Co
PI9701877-5	Atazanavir	Compound	Novartis AG
PI9607625-9*(WO9628465A1)	Darunavir	Compound	G.D. Searle & Co.

*Note:* \* Not available in the Espacenet version applied in Brazil

In relation to HIV/AIDS, 10 patents were found in the initial search by title and abstract. Five exclusions were made because: the patent was abandoned (one), it was not feasible to download the document (one), the patents related to diagnosis (two) and the indication was for herpes (one). In the end, five patents related to ARVs, as shown in table 6.

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<sup>46</sup> Brazil, Ministry of Health *Acesso universal no Brasil: Cenário atual, conquistas, desafios e perspectivas* (2010). Available from [http://www.aids.gov.br/sites/default/files/publicacao/2011/acesso\\_universal\\_brasil\\_ort\\_pdf\\_68184.pdf](http://www.aids.gov.br/sites/default/files/publicacao/2011/acesso_universal_brasil_ort_pdf_68184.pdf). Accessed on 15 January 2011.

It is also important to note that all patents granted were also approved by ANVISA. The number and scope of claims approved by INPI and ANVISA were not accessible, hence limiting the evaluation of the quality of patent examination.

In relation to lamivudine, the patent is for a formulation (oral solution). Two formulations of this medicine – 150mg tablets and an oral solution – are provided in Brazil and both are locally produced. According to ANVISA’s documentation, this patent went to the Agency twice, suggesting that there may have been restrictions to the scope of claims requested by the company. However, the patent protection does not seem to block the production of generic versions locally.

The didanosine case is emblematic, as the active ingredient is in the public domain, thus allowing the government to locally produce the generic version of a powder for oral solution. However, the formulation of an enteric-coated capsule is considered better from the patients’ perspective, as it can be taken once a day. The patent granted in Brazil relates to an enteric coated formulation, blocking the government from procuring generic versions available on the international market (Aurobindo, Cipla and Ranbaxy) or to produce it locally.<sup>47</sup>

Atazanavir is marketed by Bristol Meyer Squibb (BMS), but the first basic patent related to the compound was applied for by Novartis and this is the one which creates a monopoly situation in Brazil. BMS made several subsequent applications. The correspondent basic patent filed by Novartis was contested by civil society groups in India on the grounds of lack of novelty<sup>48</sup>. ANVISA gave its consent to this patent in 2004, at the very beginning of the “prior consent” mechanism.

However, the lack of novelty of this atazanavir patent could be considered in a review or through the presentation of a post-grant opposition. Atazanavir is one of the most expensive ARVs procured by the government, accounting for 22.38 per cent of the expenditures of the

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<sup>47</sup> Medecins Sans Frontières, *Untangling the Web of Antiretroviral Price Reductions*, (Geneva, July 2011). Available from <http://utw.msfaaccess.org/drugs/didanosine>.

<sup>48</sup> Medecins Sans Frontières, *Untangling the Web of Antiretroviral Price Reductions*, (Geneva, July 2011). Available from <http://utw.msfaaccess.org/drugs/atazanavir>.

total ARVs procured by the government by 2007.<sup>49</sup> The monopolistic situation does not only affect prices, but also the possibility to quickly obtain versions available in the international market to overcome shortages. For example, in February 2011, shortages of atazanavir were reported in different Brazilian states – Rio Grande do Sul and São Paulo.<sup>50</sup>

Darunavir was included in the national guideline in 2008 and the annual cost per patient of this medicine, boosted with ritonavir, at that time was US\$6,037.<sup>51</sup> The patent granted relates to the basic compound and so far there is no generic version available on the international market. The final examination by ANVISA was done in 2007.

The few patents for ARVs in the scope of the research can be explained by the fact that several key ARVs were patented under the “pipeline mechanism”. As shown in table 8, lopinavir/ritonavir, abacavir and efavirenz (compulsory licensed in 2007) were patented under this mechanism. Amprenavir and nelfinavir were also patented under the pipeline, but were recently excluded from the national guideline.

A study (Hasenclever *et al*, 2010) calculated the hypothetical financial losses caused by the adoption of the pipeline mechanism in the case of government purchases of five antiretroviral drugs (ARVs), during the period 2001-2007. The results show that, due to the granting of unmerited patent protections for these medicines, the Brazilian State paid an additional US\$420 million, when prices were compared with the World Health Organization’s minimum prices, and an extra US\$519 million, when compared with the minimum prices of Doctors Without Borders (MSF) for ARVs.

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<sup>49</sup> Presentation made by Dr., Mariangela Simão, National STD/AIDS Programme, Ministry of Health – Brazil, 2008. During the XVII International Aids Conference, in México City, México.

<sup>50</sup> Available from <http://exame.abril.com.br/economia/brasil/noticias/ministro-da-saude-discute-compra-de-remedios-para-aids>.

<sup>51</sup> Information provided by Brazilian Department on DSTs/AIDS and Hepatitis (2010). [cited 2010 June 1], in *Medecins Sans Frontières, Untangling the Web of Antiretroviral Price Reductions*, (Geneva, July 2011). Available from <http://utw.msfaaccess.org/drugs/darunavir>.



Table 7

**Antiretrovirals procured by the Brazilian Ministry of Health, 2010**

<b>Locally produced (generic version)</b>	<b>Imported (under monopolistic situation)</b>
Didanosine (ddl) Powder for oral solution	Abacavir (ABC) 300mg*
Efavirenz (EFZ) 600mg*	Abacavir (ABC) Oral solution*
Estavudine (d4T) 30mg	Atazanavir (ATV) 200mg**
Estavudine (d4T) Powder for oral solution	Atazanavir (ATV) 300mg**
Indinavir (IDV) 400mg	Darunavir (DRV) 300mg**
Lamivudine (3TC) 150mg	Didanosine (ddl) EC 250mg**
Lamivudine (3TC) Oral solution Nevirapine (NVP) 200mg Saquinavir (SQV) 200mg Zidovudine (AZT) 100mg	Didanosine (ddl) EC 400mg**
	Efavirenz (EFZ) 200mg (CL)* Efavirenz (EFZ) CL Oral solution*
	Enfuvirtide (T?20) ( <i>Kit</i> )
Zidovudine (AZT) 300mg + Lamivudine (3TC) 150mg	Fosamprenavir (FPV) 700mg
Zidovudine (AZT) Injectable solution	Fosamprenavir (FPV) Oral solution
Zidovudine (AZT) Oral solution	Lopinavir/ritonavir (LPV/r) Tablet*
	Lopinavir/ritonavir (LPV/r) Oral solution*
	Lopinavir/ritonavir (LPV/r) Oral solution (baby dose)*
	Nevirapine (NVP) Oral suspension Raltegravir 400mg Ritonavir (RTV) 100mg
	Tenofovir (TDF) 300mg

*Note:* \* Medicines with patents protected under the pipeline mechanism.

\*\* Medicines with patents found in the present study.

*Source:* Brazil, Ministry of Health, Acesso universal no Brasil: Cenário atual, conquistas, desafios e perspectivas (2010).

In relation to cancer medicines, no patents were found. Although 55 patents were identified through the key-words established (“tumour”, “cancer” and “antineoplásico” and “neoplasia”), none were directly linked to a specific medicine available on the market. Two hypotheses could explain this result: (a) cancer medicines were protected under the pipeline mechanism, (b) cancer medicines had their patent applications rejected by INPI and ANVISA.

In order to test the first hypothesis, cancer medicines protected under the pipeline system were identified.<sup>52</sup> The following medicines were found: letrozole (Femara®), capecitabine (Xeloda®), topotecan (Hycamtin®), fulvestrant (Faslodex®), temozolomide/mitozolomide, epirubicin; idarubicin; 4-épi-doxorubicin tachykinin antagonists aromasin, paclitaxel, iododoxorubicin, iriffulven; hydroxymethylacylfulvene, dutasteride, raloxifene, imiquimod, imatinib, gemtuzumab ozogamicin.

When analyzing some patents not granted by ANVISA under the prior consent mechanism, it was also possible to find docetaxel, which is perhaps the most emblematic case (see box 5).

**Box 5**

**The Docetaxel case**

In 2009, the Federal Public Prosecutor (MPF) filed a lawsuit of administrative dishonesty against six public service officials of the Brazilian Patent Office (INPI), the pharmaceutical companies Aventis Pharma SA and Aventis Pharma Ltda. and their representatives and directors. The reason for such an action related to the violation of the patent on the active ingredient docetaxel trihydrate for the treatment of breast cancer. (Case number 20095101013311-3).

The MPF requested the removal of those public service officials until the end of the process, due to dishonest conduct with the purpose of illegally benefitting the pharmaceutical company. The lawsuit aimed to penalize the defendants as established by the

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<sup>52</sup> Source: [http://www.abiaids.org.br/\\_img/media/ID\\_pipeline.xls](http://www.abiaids.org.br/_img/media/ID_pipeline.xls).

Law of Administrative Dishonesty in ways such as losing their public jobs, payment of a fine, and suspension of political rights, and Aventis Pharma SA and their subsidiary through the compensation of the damage caused and of further contracts with a public entity.

The lawsuit is a consequence of a complaint made by the Brazilian private company Quiral Química do Brasil to the Public Prosecutor in 2005, about irregularities by INPI when granting the patent to Aventis Pharma in 2002. According to investigations done by MPF, the defendants worked against what was established by the law, such as delaying some steps, issuing dubious and vague certificates and violations to the industrial property legislation. Among those violations, INPI granted the patent when ANVISA rejected it within the scope of the prior consent mechanism.<sup>53</sup>

#### **VII.4 The Case of National Pharmaceutical Companies**

Patent applications made by pharmaceutical manufacturers members of Abifina were searched on the INPI website based on their names. All applications were included in the research, even those not related to pharmaceuticals. A total of 198 applications were found, among which only 7.5 per cent (15) were granted, 14.6 per cent (29) rejected and 21.6 per cent (36) were abandoned. The remaining applications are pending, and most of them due to lack of payment or lack of presentation of a representative.

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<sup>53</sup> Fontes: Agencia Brasil. Ministério Público investiga concessão de patente sobre medicamento. 18 de junho de 2009. Available from <http://www.diariodasaude.com.br/news.php?article=ministerio-publico-federal-investiga-concessao-patente-sobre-medicamento&id=4232>; e Ministério Público Federal. MPF/RJ processa funcionários do INPI e da Aventis. 16 de junho de 2009, available from <http://www.jusbrasil.com.br/noticias/1342171/mpf-rj-processa-funcionarios-do-inpi-e-da-aventis>.

In relation to the 15 granted patents, it is worth noting that 12 are held by the Oswaldo Cruz Foundation, three were protected under the pipeline mechanism, and two related to tropical infectious diseases.

Although the empirical data of the current study is limited, it is possible to raise some hypotheses for future research regarding the very few patents granted to Brazilian manufacturers in the pharmaceutical field:

- There is still a very incipient capacity of innovating in this sector in the country;
- There is not much knowledge on how to use the patent system as a means of appropriation; Innovation in the country should be thought of and stimulated in another ways, as the patent system is not the best option to reward innovation.

The number of patents has been considered as an indicator of innovation, as reflected, for example in the Frascati Manual (OECD, 2007). However, in the case of the pharmaceutical sector, this is not the proper indicator to measure innovation, as companies usually file several applications (for salts, polymorphs, formulations etc.) which aim to cover a specific product in order to extend the monopoly and create barriers against generic competition. This is known as the “evergreening” strategy.

It is also worth mentioning that in the case of the pharmaceutical sector, several studies show that the strengthening of the patent protection system in the last 15 years was not followed by an increased rate of innovation, which is rather decreasing. There is an increase in the number of “me-too” drugs – pharmaceutical active ingredients with the same molecular structure already established in a therapeutic group and the same mechanism of pharmacological action – with little or no therapeutic improvement.

A survey published in April 2005 by *La Revue Prescrire* concluded that 68 per cent of the 3,096 new products approved in France between 1981 and 2004 did not represent “anything new” compared to products already available. Similarly, a scientific journal, the *British Medical Journal*, published a study indicating that less than 5

per cent of all medicines recently patented in Canada could be considered as real innovations.

Moreover, a detailed analysis of hundreds of new medicines approved by the United States Food and Drug Administration (FDA), between 1989 and 2000, showed that 75 per cent did not represent therapeutic benefits compared to products already on the market. A recent report (EC, 2008) from the European Commission shows a decrease in the number of new chemical entities (NCE) registered in the region between 1990 and 2007 (51 NCE in 1991 to 21 in 2007).

So, the question to be asked by developing countries like Brazil is: what is the proper model to be adopted to stimulate innovation in the pharmaceutical sector which really addresses public health needs?

The importation of the Bayh-Dole model to Brazil should be further investigated, as the patent system should not be an end in itself, especially considering that the costs for managing the system are high and do not potentially translate into licenses and products delivered to the public health system.

A recent study published in *PLOS Biology* (2008) shows some evidence against the Bayh-Dole model even in the United States. For example, according to the authors, “in 2006, US universities, hospitals, and research institutions derived US\$1.85 billion from technology licensing compared to US\$43.58 billion from federal, state, and industry funders that same year, which accounts for less than 5 per cent of total academic research dollars.” They also indicated that “a recent econometric analysis using data on academic licensing revenues from 1998 to 2002 suggests that, after subtracting the costs of patent management, net revenues earned by US universities from patent licensing were “on average, quite modest” nearly three decades after the Bayh-Dole model took effect. This study concludes that “universities should form a more realistic perspective of the possible economic returns from patenting and licensing activities”.









## **VIII. CONCLUSIONS**








The current patent system in Brazil shows a lack of transparency and inadequate application of the law, leading to the creation of legal uncertainty that affects the implementation of policies on access to medicines.

Although further studies should be conducted to examine whether the current policy on innovation in the local pharmaceutical sector will benefit the health system, it is already possible to raise questions on the role of patent protection as a means of stimulating innovation.










The information obtained from the local companies covered by the study suggests that they are not using the patent system as a means to appropriate their own developments. This might bring two different perspectives: (a) the innovative capacity of the country in the pharmaceutical field is still incipient; (b) most investments by those companies are oriented to the off-patented generic market.

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# CHAPTER 4

## COUNTRY CASE STUDY: COLOMBIA

Francisco Rossi

### I. COUNTRY CONTEXT INFORMATION

#### I.1 General Information

Colombia is located in north-western South America.<sup>1</sup> The population is 45,508,205 habitants, 75.37 per cent are urban and 24.63 per cent rural;<sup>2</sup> the majority of the population is concentrated in the central western zone of the territory.

Colombia is a middle income country with \$4,990 GDP per capita. 27.9 per cent of the population makes under \$2 a day, and 16 per cent is living on less than \$1 a day, according to the Human Development Report 2009. Life expectancy at birth is 72.7 years (UNDP, 2009). 5.5 per cent of the population is 65 years-old and older (1,072,644 male and 1,410,881 female) (WHO, 2006). The dependency rate in 2010 was 43.8 for children and 8.6 for older adults.

The most prevalent pathologies include respiratory infections (especially pneumonia) and chronic pathologies such as cardiovascular disease with a rate of 130.2 per 100,000 habitants and cancer with a rate

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<sup>1</sup> It has an extension of 1,141,748 km<sup>2</sup> of land mass and 928,660 Km<sup>2</sup> of maritime platform. It is divided administratively into 32 departments. Colombia has coasts on the Atlantic and Pacific oceans, and its geography is determined by the Andes mountain range, which runs through the entire country from north to south resulting in a huge variation in climate and a rich biodiversity. Ministry of Foreign Affairs and Geographic Institute Agustín Codazzi, 2009.

<sup>2</sup> DANE projections for 2009.

[http://www.dane.gov.co/daneweb\\_V09/index.php?option=com\\_content&view=article&id=238&Itemid=121](http://www.dane.gov.co/daneweb_V09/index.php?option=com_content&view=article&id=238&Itemid=121).



of 71.6 per 100,000 habitants.<sup>3</sup> Some basic health indicators characterizing the Colombian situation are presented in table 1.

Table 1

**Basic health indicators for Colombia**

<b>Indicator</b>	<b>Value</b>	<b>Source</b>	<b>Year</b>
<b>Infant mortality</b>	17/100,000	UN Data <a href="http://data.un.org/Data.aspx?d=WHO&amp;f=inID%3aMBD10">http://data.un.org/Data.aspx?d=WHO&amp;f=inID%3aMBD10</a>	2006
<b>Total expenditure on health as a percentage of gross domestic product</b>	7.3	World Health Statistics 2009 <a href="http://www.who.int/whosis/whostat/EN_WHS09_Full.pdf">http://www.who.int/whosis/whostat/EN_WHS09_Full.pdf</a>	2006
<b>Percentage Public and private health expenditure</b>	85.4 public 14.6 private	World Health Statistics 2009 <a href="http://www.who.int/whosis/whostat/EN_WHS09_Full.pdf">http://www.who.int/whosis/whostat/EN_WHS09_Full.pdf</a>	2006
<b>Public expenditure as a percentage of total public budget</b>	17.0	World Health Statistics 2009 <a href="http://www.who.int/whosis/whostat/EN_WHS09_Full.pdf">http://www.who.int/whosis/whostat/EN_WHS09_Full.pdf</a>	2006
<b>Per Capita expenditure on health</b>	534	Human Development Report 2009 ( <a href="http://hdrstats.undp.org/en/countries/data_sheets/cty_ds_COL.html">http://hdrstats.undp.org/en/countries/data_sheets/cty_ds_COL.html</a> )	2006 US\$ PPP
<b>Physicians per 1000h</b>	1.4	World Health Statistics 2009 <a href="http://www.who.int/whosis/whostat/EN_WHS09_Full.pdf">http://www.who.int/whosis/whostat/EN_WHS09_Full.pdf</a>	2000-2007

<sup>3</sup> Ministry of Social Protection. Basic Indicators 2007. Available from [www.minproteccionsocial.gov.co](http://www.minproteccionsocial.gov.co).

Indicator	Value	Source	Year
Pharmacists per 1000h	0.08	National College of pharmacists and DANE Own calculations	2009

## I.2 The Health System in Colombia

The political constitution of 1991<sup>4</sup> which replaced the constitution of 1886 included a list of social, economic and cultural rights, new democratic participation mechanisms, justice reform, and novel instruments for the protection of human rights. With regards to the latter, it is interesting to highlight the “acción de tutela” (writ for the protection of constitutional rights) a mechanism allowing individuals to claim fundamental rights in case of their violation or limitation, and the “acción popular”, a type of class action lawsuit when collective fundamental rights are violated or limited.<sup>5</sup>

Rights recognized by the political constitution include the right to life, personal integrity, equality, intimacy, freedom of personality development, personal liberty, freedom of conscience, freedom of religion, freedom of information, the right to petition, free movement, labour rights, the right to learn and teach, the right to honour and reputation, habeas data, habeas corpus, proper process, freedom to meet, and freedom of expression and political rights.

Articles 48 and 49 state that social security is a compulsory public service, and a non-waivable right. It is the responsibility of the state to lead and to regulate the health and environmental services provision, based on the principles of efficiency, universality and solidarity. In developing these articles, the National Congress passed Law 100 in 1993 establishing the general social security system on

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<sup>4</sup> Secretary of the Senate of Colombia. Constitución Política. Available from <http://www.secretariasenado.gov.co/senado/basedoc/arbol/1001.html>. Accessed on 7 October 2010.

<sup>5</sup> Procuraduría General de la Nación. Guía de la Participación Ciudadana. [http://www.procuraduria.gov.co/html/sitio\\_guia/index.html](http://www.procuraduria.gov.co/html/sitio_guia/index.html). Accessed on 2 November 2010.

health,<sup>6</sup> and subsequently passed reform by law 1122/2007, and bylaw 1438/2011. Law 100 is based on the provision of essential services and products pertaining to health, defined in the so called “Plan Obligatorio de Salud” (POS) a compulsory health plan for every citizen, an insurance model operated by private insurers.

There are three regimens for citizens with membership to the health system:

- Contributive, which covers approximately 36 per cent of the population, financed by contributions of employers and workers (12.5 per cent of their income).
- Subsidized, for people without payment capability, which covers approximately 43 per cent of the population. The state covers the insurance cost in its totality or partially, financed by contributions and fiscal resources.
- Exceptional regimes for the armed forces, national police, teachers, the National Petroleum Company and public universities.
- Non-insured population (around 10 per cent) which receives services from public institutions of the national public network, and from some private institutions (Leguizamón, 2007).

The contributions of members of the system are made to the Solidarity and Security Fund (FOSYGA), which allocates resources based on the concept of Capitation Payment Unit (UPC). Additionally, the fund is responsible for the payment of high cost diseases and traffic accidents, and also for exceptional interventions, which are not covered under the compulsory health plan. Healthcare interventions that are community-oriented, environmental sanitation and individual interventions having high externalities are funded from tax revenue and are free for all inhabitants.

The system theoretically promotes competition among the insurers and service providers, through the free choice by users of an insurer and the competition among the entities that offer services which

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<sup>6</sup> Ley 100 de 1993. Available from [http://www.secretariasenado.gov.co/senado/basedoc/ley/1993/ley\\_0100\\_1993.html](http://www.secretariasenado.gov.co/senado/basedoc/ley/1993/ley_0100_1993.html).

are public and private, although there is a marked tendency towards privatization.

The above-mentioned principles of universality, solidarity and equity are the basis upon which Colombia has chosen a unique system that seeks to ensure that each individual can access the most effective combination of inputs (including drugs) and healing resources. The services must be the least expensive to ensure universality of access.

According to initial projections, universal coverage would have been reached by the year 2000 with a single equitable benefit plan and financial stability. Nevertheless, to date this goal has not been achieved yet. Although an assessment conducted in 2010 reported significant progress, especially in terms of increased coverage, reduced pocket spending, greater access to a first visit for the insured population and an increase in consultations, problems relating to avoidable mortality, especially maternal mortality, quality of care, barriers for accessing services, and ethical concerns raised serious questions about the performance of the system.

Although health was not considered by the Constitution as a fundamental right, but just an extension of the right to life, the Constitutional Court in case T 760 of 2008, when reviewing a writ for the protection of constitutional rights, stated that the right to health was “essential”. This ruling ordered the government to comply with a series of measures to ensure access, remove barriers and match the packages of insurance schemes.

Expenditures on healthcare increased greatly in comparison to those made under the former national health system. Nevertheless, it is noteworthy that the contributive regime is growing slower than expected, while the subsidized regime is growing faster, as is evidenced by household surveys in 1997 and 2003 and the national study of demography and health Leguizamón, 2007). This contradicts one of the fundamental assumptions of the system, and puts at risk the attainment of its principal objectives and its financial sustainability (Martínez et al., 2002).

### **I.3 Evolution of Public Expenditures on Health and Health Insurance Coverage (1980-2004)**

In 2005, the total spending per capita on health reached US\$581; approximately 7.8 per cent of GDP spent on health. Of the total health expenditure, 84.1 per cent was borne by the government, which represented 20.4 per cent of all government spending. The remaining 15.9 per cent of all health expenditures were covered by private entities, of which 7.5 per cent were out-of-pocket.

A recent study by the National University of Colombia commissioned by the Ministry of Social Protection has shown artificially inflated prices by around 800 billion pesos (about US\$400 million) of medicines included in the compulsory plan. Three health insurers belonging to the same economic group concentrated around 80 per cent of these inflated prices. The expenses allocated to FOSYGA increased from Col\$306,689.00 to Col\$150,576,938.616 in 2007 to 1,587,469.00 and 1,149,839,060.873 in 2009. It was estimated that by 2010 this amount would exceed 2 billion pesos. This points to a structural crisis that needs to be urgently addressed.

### **I.4 National Drug Policy and its Relationship with the Healthcare Social Security System**

In Colombia, the pharmaceutical policy has been based on drug selection consistent with the essential drugs policy of the World Health Organization, and the encouragement of competition through promoting the use of generic drugs.

Since the early 20's, Colombia began to develop a domestic pharmaceutical industry, which formed the basis for policies consolidated years later, with the enactment of the "generic programme", by President Guillermo León Valencia in 1963. This programme aimed to provide essential medicines at low prices (often costing up to 90 per cent less than market prices). Decree 709 of 1991, introduced the sale of essential pharmaceutical products by generic name. Current National Pharmaceuticals Policy recommends the

widespread use of medicines sold under the International Nonproprietary Name (INN).

Law 100 of 1993 in its Article 162, Decree 2200 of 2005, Article 4 of the Agreement 228 of the National Council of Social Security for Health, Agreements 3 and 8 of the Health Regulatory Commission established the requirement for prescribers to use the INN in every prescription. While generic substitution is allowed in pharmacies, the delivery of cheap drugs is not incentivized, since the pharmacies' remuneration scheme is based on a percentage of the price of sold medicines.

In 1948, Colombia developed its first list of essential medicines for the then Colombian Institute of Social Security, which at that time included only the generic names; and since 1965 it was stratified by level of care. The national essential medicines list includes more than 660 items for the treatment of diseases prevalent in Colombia. Every institution, public or private, utilizes this list. The list is updated by the Health Regulation Commission created by Law 1122 of 2007. The national essential medicines list contains four sub-lists:

- Ministry of Social Protection programmes, which are part of the basic packages whose provision is the responsibility of the state. This includes EPI (expanded programme of immunizations) and medicines for the treatment of tuberculosis, malaria, leprosy, Chagas disease, acute respiratory infection and others.
- Medicines for outpatient use.
- Medicines for hospital use only.
- Medicines for specialized use.

In 2003, the Ministry of Social Protection developed a National Pharmaceutical Policy (NPP) adopted at the end of that year. The stated objective of this policy is to optimize the use of medicines, reduce inequalities of access and assure quality. In order to improve the use of medicines, the NPP proposed actions on prescription and dispensation, boosted pharmaco-epidemiology, pharmaco-economics and pharmacovigilance, and promoted the diffusion of information to consumers.

Regarding access, the policy proposed to develop mechanisms for updating the National Essential Drugs List, assess the impact of pricing policies, improve competition through generic medicines, review the financial model and develop the supply system. Promotion and advertising, is prohibited for prescription drugs. OTC medicines are regulated by Resolution 114/2004.

There is also a long history regarding quality and safety considerations. In 1927, the Pharmaceutical Specialties Commission was created to grant marketing approval of medicines. Currently, the regulatory authority, INVIMA, is the agency responsible for such approval, for sanitary surveillance, quality of medicines and pharmacovigilance. All manufacturers must comply with good manufacturing practices. There is also a sampling programme for testing the quality of medicines.

The NPP proposed to extend GMP to all intermediates in the pharmaceutical chain, develop a model of vigilance and control, strengthen the regulatory capacities of the state and facilitate coordination between local and national authorities. It did not include any provision for the public production of strategic medicines, or references to innovation, research and development of new medicines, with the exception of some proposals for the regulation of biologics, biotechnological products, homeopathic and natural drugs. Public procurement policies give preference to local manufacturers for the supply of medicines when all other conditions are equal.

## **I.5 Pricing Policy for Medicines**

Regulations on prices of medicines include the following:

- Law 81 of 1988 (Articles 60 to 62)
- Decree 3466 of 1982
- Law 100 of 1993 (Paragraph of Article 245)
- Decree 413 of 1994
- Decree 147 of 1999
- Circular 04 of 2006 of the National Price Commission for Medicines (CNPM)

- Circular 05 of 2006 of the National Price Commission for Medicines (CNPM)
- Circular 01 of 2007 of the National Price Commission for Medicines (CNPM)
- Circular 02 of 2007 of the National Price Commission for Medicines (CNPM)
- Circular 03 of 2007 of the National Price Commission for Medicines (CNPM)

The body in charge of pricing policies is the National Price Commission, composed of the Minister of Commerce, Industry and Tourism, the Ministry of Social Protection and a delegate of the President of the Republic. Circular 04 of 2006 restructured the price policy. Before this decision, each product with three or fewer bids was subject to a direct control scheme. It was changed for a new model where every drug is under “controlled freedom” unless there is an increase in market concentration measured by the Herfindahl Hirschman index (HH), in which case a price reference model should be applied. The study used for this change to the national policy was directly financed by the pharmaceutical industry.

Currently, the pricing policy includes three regimes:

- a. The Direct Control Regime: the Commission determines the maximum public price.
- b. The Regulated Freedom Regime: the Commission determines the criteria and methodology to establish maximum prices.
- c. The Controlled Freedom Regime: producers and suppliers determine prices freely. They are required to report prices to the competent authority, periodically, following a standardized methodology.

Every medicine is currently under the Controlled Freedom Regime, except where:

- a. Government considers that it is necessary to protect public health (regulated market).
- b. The HH index is equal or superior to 0.45.
- c. There are no substitutes at the time of market entry.
- d. Information is incomplete or wrong.



## **I.6 The Pharmaceutical Market**

Apparent consumption<sup>7</sup> of medicines in Colombia was estimated at US\$2.232 billion, according to calculations by the Pharmaceutical Chamber and DANE. This consumption has shown a constant upward trend during the last decade. There is a co-payment designed to promote the appropriate use of services and medicines, to reduce overuse and to finance the system.

IMS reported a total private market of US\$1.897 billion for Colombia between the period September 2009 to September 2010, and the number of units consumed was 308,735,746. The supply chain as reported by IMS is as follows:

- The private market includes 19,378 pharmacies (6,999 independent, 2,116 from chain pharmacies and 263 from compensation funds).<sup>8</sup> In this market, medicines are financed by out of pocket expenditures.
- The institutional market, linked to the general system of social security on health, includes private and public institutions. It includes 32 insurers, 10 private insurance companies and 58 compensation funds.
- Seventy-four per cent (US\$966 million, 2004) of the total market consisted of imported medicines and 26 per cent, (US\$335 million, 2004) domestically produced medicines.<sup>9</sup>
- The growing expenditure in medicines is considered to be responsible for the crisis of the health system. Pharmaceutical expenses increased from 19.4 per cent of the Capita Payment Unit – UPC – (2004) to 27.2 per cent (2007) according to ACEMI, the insurers association.

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<sup>7</sup> Apparent consumption shows availability of a product consumed in a region or country in a period of time. It is estimated by using the national production plus the trade balance over a period of time.

<sup>8</sup> IMS Health A.G. Pharmaceutical Market. Colombia June 2010.

<sup>9</sup> Estudio de la política de Precios de medicamentos en Colombia, *Econometría*, 2005. (Study of the Price of Medicines in Colombia).

## **I.7 Science, Technology and Innovation**

The national system of science, technology and innovation (ST&I) seems well designed, but it is still weak and with some operational deficiencies, including the lack of articulation among different sectors and entities.

There is no single example of a complete cycle of discovery, research and development of pharmaceuticals in Colombia, although there are capabilities in every phase of the process in the country.

In particular, there is a lack of therapeutic options to face public health challenges such as tuberculosis, malaria, Chagas, leishmaniasis and dengue, to mention just a few.

Law 1286 of 2009 transformed COLCIENCIAS into an administrative department, and strengthened the national system of science, technology and innovation. Although there are some experiences in clinical research, there is no articulation between COLCIENCIAS and INVIMA.

## **I.8 Intellectual Property Protection**

The intellectual property regime in Colombia was established in 1834 by Act 10. It referred exclusively to the production of literary and musical works, drawings, maps, paintings, and designs. The authors could seek protection from the governor of the province of their place of residence by submitting the title of the work or composition, for registration and issuance of a certificate of ownership, which gave the right to enjoy exclusivity as defined by the law. The certificate of ownership indicated the name of the province where the right was granted, the petitioner's name, the title of the work and the term of exclusivity, which initially was 15 years, from the date of issuance, renewable for another 15 years provided that the request for renewal was made 6 months prior to expiration.

The advent of the modern patent system in Colombia has its roots in Law 15 of 1848, "Law of Patents, Improvement of Machinery

and Industrial Products." This law provided for exclusive rights to manufacture or sell, for a period of five to twenty years, the protected product. It included industrial developments which were not protected in the previous system.

A new amendment to the patent law (Law 35 of 1869) was made to promote the commercial exploitation of patented products. The system was reformed again by Law 31 of 1925, which provided for a patent term of 20 years, divided into two periods of 10 years, and established the first limitations on the granting of patents in certain sectors, especially for inventions contrary to health and public hygiene, safety, or morality.

Through Law 16 of 1968, Congress gave the President special powers to amend the industrial property legislation in force. These powers were used in 1971 with the issuance of Decree Law 410 by means of which the Code of Commerce whose title II on patent protection was adopted.

Title II of the Commercial Code concerning industrial property, was amended by Decision 85 of the Cartagena Agreement incorporated into national legislation by Decree 1190 of 1978 and later by Decisions 311, 313, 344, 486, 632 (which interpreted article 66 of Decision 486) and 689 (which allowed member countries to adopt certain measures).

Decision 344 of 1994, excluded from patentability inventions related to the products included in the list of Essential Medicines of the World Health Organization.

Law No. 170 of 1994 approved the Marrakesh Agreement, which mandates the implementation of the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement).

The countries belonging to the Andean Community of Nations (CAN) adapted their legislation to the TRIPS Agreement on intellectual property through Decision 486 of 2000.

The Paris Convention for the Protection of Industrial Property was originally signed by 11 states in 1883 and amended in Brussels in

1900, in Washington in 1911, in The Hague in 1925, in London in 1934, in Lisbon in 1958 and in Stockholm in 1967. It was adopted by Colombia by Act 178 of 1994 (accession, 3 June 1996).

Decisions taken by Colombia on intellectual property, especially after 1990, have largely been influenced by pressures and demands from the United States and other developed countries in the context of trade negotiations.

A central element in the exercise of those pressures has been the Special Section 301 of the US Trade Act, which authorizes the United States Trade Representative (USTR) to review countries' practices on intellectual property protection and enforcement and to eventually apply trade retaliations.

Pressures were also exerted on Colombia regarding its intellectual property system through the Andean Trade Preference Act (TPA), the commercial component of the programme of the War on Drugs that President George Bush Senior issued on 4 December 1991. TPA was replaced by the Andean Trade Promotion and Drug Eradication Act (ATPDEA) signed on 6 August 2002 by President George Bush Junior.

Pharmaceutical companies members of AFIDRO, the association of research based pharmaceutical laboratories in Colombia, affiliated to PhRMA, have been active in pursuing USTR intervention against Colombia. Colombia was forced to issue Decree 2085 of 2002, which prevents a third party from registering a product containing a new active ingredient relying on the safety and efficacy data of the originator. This modality of "data exclusivity" is questionable from public health perspective focused on the right to get access to medicines.

After enforcement of Decree, 2085 which enshrines the particular interpretation of the US pharmaceutical industry on WTO commitments under article 39.3 of the TRIPS Agreement, Colombia was moved from the USTR "Priority Watch List" to the "Watch List", that is, the list of those with "very bad" behaviour to those with "just bad" behaviour.

Pressures exerted during the negotiation of an FTA with the USA also played an important role in changes introduced to the price control system of the country. The public message from the Government of Colombia suggests that price control measures were implemented as a counterweight to intellectual property provisions, as established by Decree 2085 and the obligations under the future Colombia Trade Promotion agreement.

So far, the Colombian Government has not recognized the negative effects of intellectual property rules on access to medicines and its response to civil society has focused on mitigating the potential effects of the FTA. The Government's proposed measures have a strong emphasis on trade and financial aspects such as:

1. An increase in the value of contributions to the health system.
2. Hospitals to be declared "free zones".
3. Using the strategy of partial subsidies to finance the Compulsory Health Plan.
4. Strengthening INVIMA (especially to meet requirements related to sanitary and phytosanitary measures for the export of meat and milk).
5. Possible creation of a National Intellectual Property Institute.
6. Control of drug prices.

The first two measures benefit the consumers of medicines but also, and principally, the pharmaceutical companies by providing additional resources to pay more for needed medicines, and this does not necessarily mean a real expansion of coverage. The third proposal suggests a potential cut in health benefits, in response to the lack of resources.

The fourth proposed measure is important, but obviously has a commercial rather than a health objective. The creation of a National Intellectual Property Institute is just a proposal. Its role in protecting public health would be even more marginal than it is today under the Superintendency of Industry and Commerce.

The sixth proposal is extremely worrisome because multinational drug companies are pushing to eliminate price controls and have taken an important step with the new drug pricing circular (Circular 4 of 2006).

## **II. THE COLOMBIAN PATENT SYSTEM**

According to the TRIPS Agreement, a patent has a minimum duration of 20 years, which means that during that period, no one else can – without the patent owner’s consent – manufacture, sell, use or import the product under patent or manufacture the product by the patented method. An existing patent also prevents the patenting of identical or equivalent subject matter.

There is a controversy concerning the implementation of the 20-year term of a patent. Although it is true that there is a need to foster research and development of new drugs, it is also essential that they become rapidly available to save lives from the moment of their entry into the market and not after the expiry of a 20-year period.

Intellectual property is deemed to encourage innovation through the creation of exclusivity, and thereby protecting the inventor against market failure. This failure exists since the drugs are not necessarily difficult to replicate or imitate (the term “copy” has legal connotations so its use is not recommended). The research and development of new drugs would be a very bad business if the very next day someone could introduce a "reproduction" without all the costs of R&D. At the same time, patents create monopolies, limit competition and allow right holders to charge high prices, which in the long run limit access and create distortions in consumption.

Recent evidence suggests that the patent system is facing a crisis. On the one hand, while the number of granted patents is increasing worldwide, the number of new chemical entities is falling. The quality of innovation is decreasing and the claimed cost of new drugs is growing at an alarming rate. This is a global phenomenon and a

growing concern, not only for developing countries but for developed countries as well.

The patent system can be understood as an agreement between society and inventors, in which society temporarily sacrifices access, for innovation. Patents are national, international patents do not exist. In this sense, each country has the possibility to implement its patent system in the context of its policies on science and technology, to promote local industry, to stimulate foreign investment and, certainly, to protect public health.

Pharmaceutical patents should only be granted for inventions that satisfy the criteria of novelty, inventive step and industrial application. However, global attention has been drawn to the risks of a lax application of these criteria, generating "low quality" and broad coverage patents, especially by granting patents to minor modifications of protected products, new uses, combinations and new formulations of known drugs. This permits the extension of the monopoly period of the right holder and delays market entry of generic drugs. In contrast, the number of new chemical entities developed has declined dramatically over the last ten years.

There is, in fact, growing evidence regarding the proliferation of patents for minor modifications of existing products in both developed and developing countries. The number of patents for simple changes in chemistry and development of existing pharmaceutical products (for example, polymorphs, combinations, dosage forms, and isomers) has steadily increased. Thousands of patents are granted each year for these minor innovations. In addition, most new drugs approved in 1982-1991 by the FDA are "me-too" drugs, that is, drugs that do not have a new therapeutic effect, which are often promoted by pharmaceutical companies as substitutes for existing drugs, but at a much higher price.

The use of patents to exclude generic competition can prevent access to affordable medicines and may constitute a major obstacle to the exercise of the right to health. The objectives of the TRIPS Agreement include stimulating innovation and promoting technology transfer while providing a mechanism to benefit society. In this sense,

every country, both developed and developing, should build its patent system in a manner that encourages innovation, investment in R&D and preserves a robust public domain.

Developing countries keen to promote local innovation face a political dilemma regarding the level of the inventiveness required to grant patents. A key question is whether the application of low patentability criteria would provide incentives for innovation by domestic firms and whether such incentives would offset the costs associated with the proliferation of patents on minor technical changes. This does not seem to be the case indeed – local innovation in pharmaceuticals in Latin America is minimal despite the fact that the number of patents has significantly increased.

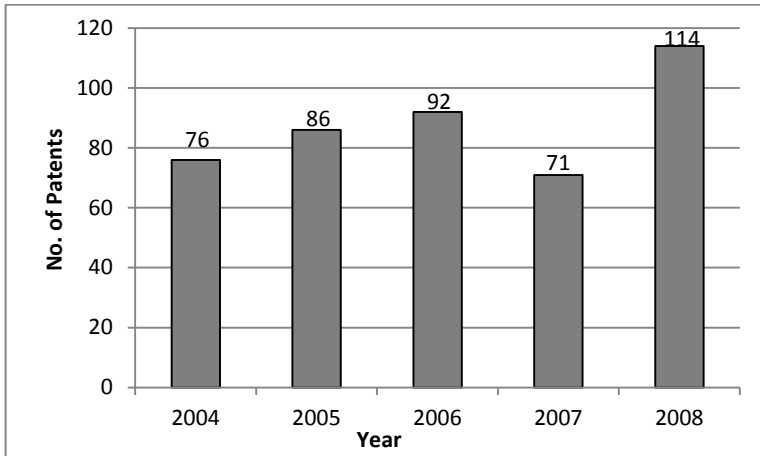
In Colombia, under Decision 85 of 1974 of the Cartagena Agreement, only processes for obtaining pharmaceutical products were patentable but not the products themselves. However, with Decision 341 and later Decision 344 of 1994, products became patentable subject matter, except those on the list of Essential Medicines of the World Health Organization. In 2000, following Decision 486 of the Andean Community – which adapted the legislation to the TRIPS Agreement – the patenting of essential medicines was also allowed. An increasing number of companies rely on patent protection in Colombia. The growth rate of grants in the pharmaceutical industry has been relatively constant in recent years as shown in figure 1.

In the period 2004-2008, 439 granted patents were identified. It is noteworthy that all these patents were granted to foreign multinational firms, notably from the United States, Germany, Switzerland and France.



Figure 1

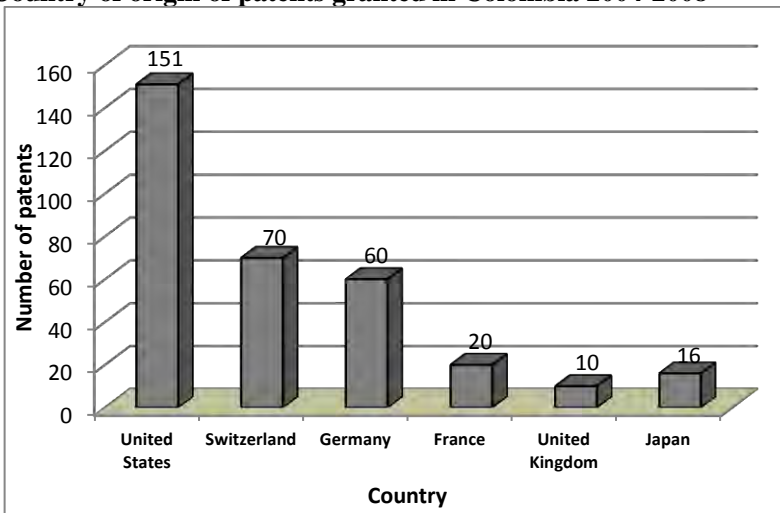
**Patents Granted in Colombia 2004-2008**



Source: Authors. Survey data.

Figure 2

**Country of origin of patents granted in Colombia 2004-2008**



Source: Authors. Survey data.

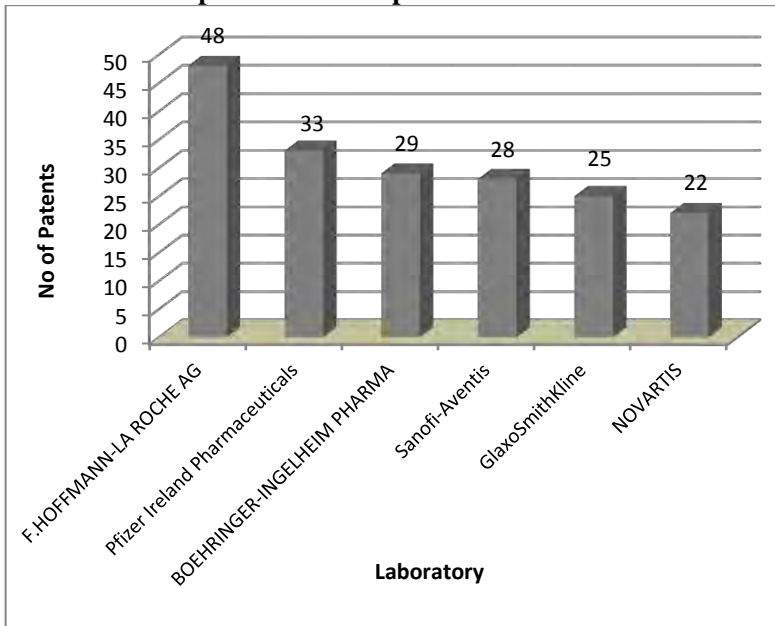
According to the country of origin of patent owners, 34 per cent were from the United States, followed by Switzerland and Germany. It is clear that these countries are internationally recognized for their R&D activities. They are home to large pharmaceutical companies such as F. Hoffmann-La Roche (Switzerland), which owns 11 per cent of all the patents, followed by Pfizer (United States) and Boehringer Ingelheim (Germany) with 7 per cent and 6 per cent respectively. (See figure 3).

Local enterprises obtained just two patents in that period. The subject matter referred to excipients and not to an active ingredient, since Colombian laboratories do not carry out research on the synthesis of such ingredients.

In order to engage in the production of generic drugs, domestic laboratories have had to seek strategic alliances and technology transfer contracts with patent owners, against the payment of royalties.

Figure 3

**Patent holders of pharmaceutical patents in Colombia 2004-2008**



Source: Authors. Survey data.

Colombia is considered a country where patents are granted only to genuine innovations that fully meet technical and legal requirements. However, in recent years the number of grants has increased, possibly due to relaxation of the application of patentability criteria. A 2011 report from the patent office (Superintendency of Industry and Commerce – SIC), indicates a 26 per cent increase in the number of patents granted, most of them PCT. This may be the result of the strategy applied to encourage the use of intellectual property and stimulate innovation, consisting of a reduction of tariffs and a more relaxed review of applications.

Patents granted in Colombia reflect a particular interest in products that act on the central nervous system, as well as antineoplastic and immune-modulating products. It reflects a bias towards products for the most lucrative markets, and little research outputs to address the health problems of developing countries, particularly neglected diseases.

Table 2

**Patents granted in Colombia according to therapeutic class**

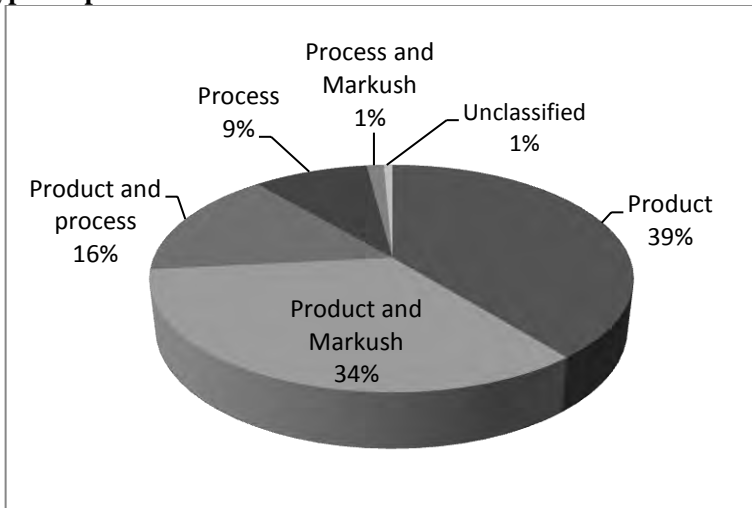
<b>Therapeutic class</b>	<b>Number of patents</b>
N - Nervous system	87
Unclassified	79
L - Antineoplastic and immunomodulating agents	57
J - Anti-infectives for systemic use	39
C - Cardiovascular system	37
A - Alimentary tract and metabolism	36
M - Musculoskeletal system	32
B - Blood and blood forming organs	17
R - Respiratory system	15
G - Genito-urinary system and sex hormones	14
V - Various	9
P - Antiparasitic products, insecticides and repellents	9
D - Dermatologicals	6
H - Systemic hormonal preparations, excluding sex hormones and insulin	1
L01 - Antineoplastics	1

*Source:* Authors. Survey data.

A large proportion of granted patents do not reveal the therapeutic indication neither in the title nor in the claims. Only in 20 per cent of cases was the therapeutic indication properly indicated. Fourteen per cent of them could be used for more than one indication. (See figure 4).

It is also important to note the high number of Markush claims. This may result in later applications for “selection patents” leading to “evergreening”. It could also lead to an obstruction of lines of research since these types of claims may include millions of molecules.

Figure 4  
**Types of patent claims in Colombia 2004-2008**



A review of claims in granted patents determined that 79 per cent were “inappropriate”, most of them corresponding to an active ingredient (266), followed by formulations (38). This qualification was made by an expert group of pharmacists and lawyers from the Universidad de Antioquia, using the WHO-UNCTAD-ICTSD

guidelines.<sup>10</sup> Certainly, this qualification was made just for academic purposes.

The study also revealed that out of 439 patents granted in Colombia, approximately 60 per cent were no longer in force, as a result of unpaid annual maintenance fees.<sup>11</sup> The fee is minimal, suggesting that the fee itself is not the reason for failure to pay. In fact, there are only a small number of patents in effect in the Colombian market. Two hypotheses could explain this: exclusivity can be achieved by other more effective mechanisms (trade, technology barriers and regulatory barriers) or patents have been used just to block lines of research by local groups. A large number of abandoned patent applications were also found, suggesting that applicants were interested in discouraging potential competitors even when they did not intend or expect to obtain a patent.<sup>12</sup>

In this context, data on patents granted in Colombia show that one of the objectives of the patent system – to promote local innovation – is not being attained, while it is clear that some patents or patent applications are used to block local research and production.

### III. LITIGATION

There has been an important number of cases litigated on intellectual property relating to medicines in Colombia in recent years.

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<sup>10</sup> Correa, C, *Guidelines for the Examination of Pharmaceutical Patents: Developing a Public Health Perspective* (World Health Organization, International Centre for Trade and Sustainable Development, United Nations Conference on Trade and Development and the United Nations Development Programme, January 2007).

<sup>11</sup> Alix de Vergel. Superintendencia de Industria y comercio. Proyecto de Evacuación de Nuevas Creaciones. 2007-2010. Programa De Mejoramiento Del Sistema De Propiedad Industrial. Quoted in Informe Nacional de competitividad 2009 – 2010. Available from

<http://www.compite.com.co/site/informe-nacional-de-competitividad-2009-2010/>.

<sup>12</sup> Sepúlveda Joan et al. Vitae. Transparency of the pharmaceutical patent information system in Colombia. Paper for revision submitted and accepted in August 2011.

### III.1 Pre-grant Opposition

A first kind of litigation refers to pre-grant opposition, which is allowed in Colombia during the 60 days following the publication of the application. The opposition system allows the person submitting it to become a third party during the whole process of patent examination, and gives them the right to be notified of any decision, including the filing of appeals against the patent grant.

It is also possible to present information to contribute to the examination of a patent application after the expiry of the 60-day term mentioned above but, in this case, the opponent does not become a third party, and shall not be informed or notified of the decisions. In an important number of cases, this contributed to the refusal of applications (see Annex).

The 57 cases indicated in the Annex related to 17 APIs, 34 of which resulted in denial of the patent application. There is a strategy of applying for several patents around the same API. It is interesting to note that the number of successes of oppositions is very high, as summarised in table 3.

Table 3

#### Decisions on oppositions against patents around the same API

Final decision	Number	Percentage	Cumulative percentage
DENIED	34	60	60
ABANDONED	7	12	72
WITHDRAWN	8	14	86
GRANTED	8	14	14

In table 3, “denied” means that the process continued, and at the end of the examination, the authority decided not to grant the patent. “Abandoned” means that the authority asked the applicant to present additional information to answer the questions or arguments presented by the opponent, and a satisfactory response was never given. “Withdrawn” means that the applicant decided to withdraw the application and stop the process; and “granted” means that, at the end of

the process, the authority granted the patent despite the arguments of the opponent.

The second kind of litigation has to do with cases in which one party requires the State Council (Consejo de Estado, the highest tribunal on these matters) to overturn an administrative decision of the patent office. Only a few of this type of cases have been resolved, since the procedures are very long. Table 4 shows a sample of these cases, all of them still pending.

Table 4

**Cases filed before the State Council**

<b>API</b>	<b>Date of filing before the State Council</b>	<b>Subject matter of refused patent</b>
Montelukast	2005-0319	Fixed dose combination
Moxifloxacin	2006-0139	Pharmaceutical formulation
Moxifloxacin	2005-0065	Pharmaceutical formulation
Atazanavir	2007-149	Salt
Ritonavir	2005-0078	Polymorph
Rosiglitazone	2006-163	Polymorph
Rosuvastatin	2007-0086	Pharmaceutical formulation
Ertapenem	2002-363	Pharmaceutical formulation
Didanosine	2005-202	Pharmaceutical formulation
Risedronate	2009-095	Process of obtainment
Rosiglitazone	2008-244	Therapeutic method
Celecoxib	2006-0007	Pharmaceutical formulation
Clopidogrel	N/A	Method of obtainment

<b>API</b>	<b>Date of filing before the State Council</b>	<b>Subject matter of refused patent</b>
Sildenafil	2000-6608	Method of obtainment Therapeutic method
Valsartan	2004-0016	Pharmaceutical formulation
Rosuvastatin	2007-0086	Pharmaceutical formulation
Gabapentina	N/A	Therapeutic method
Escitalopram	N/A	Pharmaceutical composition
Celecoxib	N/A	Fixed dose combination
Drospirenona	N/A	Therapeutic method
Drospirenona	N/A	Pharmaceutical composition
Granisetron	N/A	Therapeutic method
Atomoxetina	N/A	Therapeutic method
Ceterizina	N/A	Fixed dose combination
Metformina	N/A	Fixed dose combination/ Pharmaceutical composition
Risedronato	2009-095	Methods of obtainment
Topiramato	N/A	Salt
Zopiclone	N/A	Pharmaceutical formulation
Ibandronato	N/A	Treatment method
Olanzapina	N/A	Hydrated Crystalline form
File 97-054-849 Olanzapina	N/A	Fixed dose combination
Olanzapina	N/A	Polymorph
Olanzapina	N/A	Polymorph
Olanzapina	N/A	Pharmaceutical form



It is interesting to note that most of these litigations are the result of a stringent application of the inventive step, since most of the applications corresponded to variations of known molecules. The last category of litigation corresponds to cases of patent infringements and the requests of provisional injunctions to prevent allegedly imminent violation of patents. We found three cases of this type, all of them related to the Lopinavir/ritonavir patent, owned by Abbott laboratories, which was the object of a compulsory license request from civil society organizations in 2008.

The first one corresponds to a lawsuit by Abbott against Biotoscana, a local branch of CIPLA. Biotoscana obtained marketing approval and Abbott claimed that it constituted an imminent patent violation. Although in Colombia the “Bolar exemption” is recognized, the judge decided to grant an injunction and to suspend the registration. Biotoscana was finally penalized with litigation costs although no damages were awarded since the product was never commercialized.

The second and third cases relate to similar lawsuits brought by Abbott against Ranbaxy and Cipla, represented in Colombia by Eliptica Medica. They had submitted applications for marketing approval of Lopinavir/ritonavir, and with similar arguments, Abbott applied for a provisional injunction. To date a final decision is still pending but the court has ordered INVIMA to suspend the study of the application in both cases. If successful, these lawsuits will create a kind of “linkage” between drug registration and patent protection.

## ANNEX

## Oppositions to Patent Applications in Colombia 2001-2010

<b>Application number</b>	<b>INN</b>	<b>Date of application</b>	<b>Applicant</b>	<b>Type</b>	<b>Date of filing</b>	<b>Final result of opposition for the patent application</b>
99-030-159	Gabapentin	1999-05-14	Warner Lambert Company	Pre-grant opposition	25/10/01 24/01/02	DENIED
99-048-774	Gabapentin	1999-08-02	Laboratories Prographarm	Pre-grant opposition	25/10/01 20/02/02	ABANDONED
98-047-006	Gabapentin	1998-08-18	Warner Lambert Company	Extemporaneous information	18/06/02	DENIED
99-058-376	Metformin	1999-09-15	Bristol-Myers Squibb Company	Pre-grant opposition	29/05/02 28/08/02	DENIED
99-071-573	Metformin	1999-11-12	Smithkline Beecham P.L.C.	Pre-grant opposition	29/07/02 24/10/02	DENIED
99-070-009	Metformin	1999-11-05	Warner Lambert Company	Pre-grant opposition	29/07/02 25/10/02	DENIED

<b>Application number</b>	<b>INN</b>	<b>Date of application</b>	<b>Applicant</b>	<b>Type</b>	<b>Date of filing</b>	<b>Final result of opposition for the patent application</b>
03-007-756	Metformin	2003-02-03	Merck Patent GmbH	Pre-grant opposition	30/06/04 18/11/04	ABANDONED
98-005-805	Oxcarbazepine	1998-02-05	Novartis Ag	Extemporaneous information	23/05/02	DENIED
98-057-677 A	Oxcarbazepine	1998-10-05	Novartis Ag.	Extemporaneous information	21/03/02	DENIED
98-057-677 B	Oxcarbazepine	1998-10-05	Novartis Ag	Pre-grant opposition	28/01/01 & 26/04/02	DENIED
00-058-801	Rosuvastatin	2000-08-04	AstraZeneca Ab	Extemporaneous information	28/06/06	DENIED
04-117-654	Topiramato	2004-11-23	Ortho-Mcneil Pharmaceutical, Inc.	Pre-grant opposition	04/07/06 & 29/01/07	ABANDONED
96-037-512	Atorvastatin	1996-07-17	Warner-Lambert Company	Extemporaneous information	19/04/02	GRANTED
96-037-513	Atorvastatin	1996-07-17	Warner-Lambert Company	Extemporaneous information	30/11/01	DENIED
96-037-514	Atorvastatin	1996-07-17	Warner-Lambert Company	Extemporaneous information	30/11/01, 05/03/02, 17/10/02 & 20/11/02	DENIED

<b>Application number</b>	<b>INN</b>	<b>Date of application</b>	<b>Applicant</b>	<b>Type</b>	<b>Date of filing</b>	<b>Final result of opposition for the patent application</b>
98-049-138	Atorvastatin	1998-08-27	Pfizer Products Inc.	Extemporaneous information	13/06/02	GRANTED
98-049-139	Atorvastatin	1998-08-27	Pfizer Products Inc.	Extemporaneous information	14/06/02 & 05/03/03	WITHDRAWN
98-069-227	Atorvastatin	1998-11-24	Warner Lambert Company	Extemporaneous information	19/02/02	DENIED
99-058-374	Atorvastatin	1999-09-15	Bristol-Myers Squibb Company	Pre-grant opposition	25/02/06 & 28/08/02	DENIED
00-048-079	Atorvastatin	2000-06-27	Bayer Aktiengesellschaft	Pre-grant opposition	25/06/02 & 20/09/02	DENIED
99-062-951	Atorvastatin	1999-10-05	Novartis Ag	Pre-grant opposition and Extemporaneous information	25/06/02, 20/09/02 & 05/09/03	DENIED
99-057-639	Atorvastatin	1999-09-10	Pfizer Products Inc.	Pre-grant opposition	29/07/02 & 24/10/02	GRANTED
00-016-008	Atorvastatin	2000-03-06	Merck & Co., Inc.	Pre-grant opposition	29/07/02 & 24/10/02	ABANDONED
00-038-315	Atorvastatin	2000-05-24	Pfizer Products, Inc.	Pre-grant opposition	24/09/02 & 13/12/02	DENIED

<b>Application number</b>	<b>INN</b>	<b>Date of application</b>	<b>Applicant</b>	<b>Type</b>	<b>Date of filing</b>	<b>Final result of opposition for the patent application</b>
00-029-421	Atorvastatin	2000-04-24	R. Preston Mason	Pre-grant opposition	24/09/02 & 13/12/02	DENIED
99-075-209	Celecoxib	1999-11-30	G.D. Searle & Co	Extemporaneous information	02/11/01	DENIED
00-033-396	Celecoxib	2000-05-10	Pfizer Products, Inc.	Pre-grant opposition	24/09/02 & 13/12/02	DENIED
00-045-172	Celecoxib	2000-06-16	Pfizer Products Inc.	Pre-grant opposition	26/11/02	WITHDRAWN
00-063-084	Celecoxib	2000-08-23	Pfizer Products Inc.	Pre-grant opposition	26/11/02 & 21/02/01	DENIED
01-087-299	Celecoxib	2001-10-10	Pharmacia Corporation	Pre-grant opposition	28/04/04	WITHDRAWN
04-042-439	Celecoxib	2004-05-07	Pharmacia Corporation	Pre-grant opposition	25/05/06 & 27/12/06	ABANDONED
99-37210	Clopidogrel	1999-06-15	Sanofi-Synthelabo	Extemporaneous information	19/07/04	DENIED
98-026-855	Clopidogrel	1998-05-13	Sanofi	Extemporaneous information	13/06/02, 19/11/02 & 22/04/03	DENIED
00-096-726	Desloratadine	2000-12-20	Schering Corporation	Extemporaneous information	16/03/07	GRANTED








<b>Application number</b>	<b>INN</b>	<b>Date of application</b>	<b>Applicant</b>	<b>Type</b>	<b>Date of filing</b>	<b>Final result of opposition for the patent application</b>
00 096 727	Desloratadine	2000-12-20	Schering Corporation	Extemporaneous information	16/03/07	DENIED
01-109-552	Desloratadine	2001-12-21	Mcneil-Ppc, Inc.	Pre-grant opposition	30/07/04 & 22/10/04	DENIED
00-051-031	Escitalopram	2000-07-07	H. Lundbeck A/S	Extemporaneous information	20/04/05	DENIED
03-062-583	Escitalopram	2003-07-23	H. Lundbeck A/S	Extemporaneous information	28/06/06	WITHDRAWN
00-068-859	Orlistat	2000-09-12	F. Hoffmann-La Roche A.G.	Pre-grant opposition	25/10/02 & 24/01/03	GRANTED
98-005-480	Orlistat	1998-02-04	F. Hoffmann-La Roche Ag	Extemporaneous information	16/01/02	GRANTED
99-050-689	Orlistat	1999-08-10	F. Hoffmann-La Roche Ag.	Pre-grant opposition	29/05/02 & 28/08/02	ABANDONED
99-050-696	Orlistat	1999-08-10	F. Hoffmann-La Roche A.G.	Pre-grant opposition	29/08/02 & 26/11/02	ABANDONED
00-068-855	Orlistat	2000-09-12	F. Hoffmann-La Roche Ag.	Pre-grant opposition	29/01/03& 25/04/03	GRANTED
00-039-187	Rofecoxib	2000-05-26	Pfizer Products, Inc.	Pre-grant opposition	26/11/02	WITHDRAWN

<b>Application number</b>	<b>INN</b>	<b>Date of application</b>	<b>Applicant</b>	<b>Type</b>	<b>Date of filing</b>	<b>Final result of opposition for the patent application</b>
99-030-493	Sildenafil	1999-05-18	Pfizer Inc.	Pre-grant opposition	25/10/01 & 24/01/02	WITHDRAWN
99-038-978	Sildenafil	1999-06-22	Pfizer Research And Development Company	Pre-grant opposition	25/11/01 & 19/06/02	DENIED
99-066-970	Sildenafil	1999-10-22	Pfizer Research And Development Company, N.V./S.A	Pre-grant opposition	29/08/02 & 26/11/02	DENIED
99-064-776	Sildenafil	1999-10-12	Pfizer Research And Development Company N.V./S.A	Pre-grant opposition	29/07/02 & 24/10/02	DENIED
99-066-723	Sildenafil	1999-10-21	Pfizer Products, Inc.	Pre-grant opposition	29/07/02 & 10/03/04	DENIED
99-081-563	Sildenafil	1999-12-30	Pharmacia & Upjohn Company	Pre-grant opposition	29/07/02	WITHDRAWN
00-056-997	Sildenafil	2000-07-28	Pfizer Products Inc.	Pre-grant opposition	19/12/03 & 25/03/03	DENIED
00-082-090	Sildenafil	2000-10-27	Pfizer Inc.	Pre-grant opposition	29/01/03 & 25/04/03	DENIED

<b>Application number</b>	<b>INN</b>	<b>Date of application</b>	<b>Applicant</b>	<b>Type</b>	<b>Date of filing</b>	<b>Final result of opposition for the patent application</b>
99-052-292	Tegaserod	1999-08-18	Novartis Ag.	Extemporaneous information	06/06/03	DENIED
02-091-881	Valsartan	2002-10-11	Novartis Ag	Pre-grant opposition	26/11/03 & 24/02/04	DENIED
00-024-081	Various substances	2000-04-03	Bristol-Myers Squibb Company	Pre-grant opposition	29/11/02 & 26/11/02	DENIED
02-091-883	Various substances	2002-10-11	Novartis Ag	Pre-grant opposition	26/11/03 & 24/02/04	DENIED
00-071-835	Various substances	2000-09-21	Bristol-Myers Squibb Company	Pre-grant opposition	19/12/02 & 25/03/03	GRANTED



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## **CHAPTER 5**

### **PHARMACEUTICAL INDUSTRY, THE HEALTH SYSTEM AND INTELLECTUAL PROPERTY POLICY IN INDIA**

Arti Malik

#### **INTRODUCTION**

India is considered a world leader in supplying generic medicines, covering 20 per cent of the global market share (Waning et al, 2010). The Indian pharmaceutical industry has been recognized worldwide for producing high quality pharmaceuticals at low costs.

Moreover, the Indian pharmaceutical industry has significantly contributed to the global scale up of HIV treatment; supplying more than 85 per cent of all generic antiretroviral in the world (Waning, et al, 2010). It has been instrumental in bringing down the prices of not only HIV medicines but also other lifesaving drugs by creating competition in the global market.

The growth of the Indian pharmaceutical industry has benefited from the favourable legal and industrial policy environment that prevailed between 1972 and 2005. Prior to 2005, the Indian Patents Act of 1970 did not recognize product patents on pharmaceuticals, which allowed Indian pharmaceutical companies to produce generic versions of medicines using reverse engineering processes. Moreover, the government encouraged research and development on producing active pharmaceutical ingredients by setting up public research institutes. This helped the pharmaceutical industry to expand and specialize in production of bulk drugs and formulations and emerge as a leading exporter of these products (Dhar and Rao, 2002).

However, the policy environment relating to intellectual property rights is changing rapidly. India, being a signatory to the World Trade Organization (WTO) was required to amend its patent laws to comply with WTO's Agreement on Trade Related Aspects of Intellectual Property Rights (the TRIPS Agreement). Hence, in 2005, in accordance with the TRIPS Agreement, India introduced product patent protection for pharmaceuticals. The product patent protection regime has the potential of restricting generic production of pharmaceuticals that can have far reaching consequences on access to affordable medicines. Cognisant of this possibility, India also introduced unique provisions as public health safeguards to protect against the granting of questionable patents and to promote strict standards of patentability.

There are concerns about India's continued ability to supply affordable medicines in India and the rest of the world. In addition to the concerns surrounding the impact of the product patent regime on the generic production of pharmaceuticals, there is a growing pressure on India to enter into bilateral free trade agreements that threaten to make intellectual property rights more stringent.

This chapter seeks to explore whether strong patent protection promotes innovation, especially among local companies and its impact on access to affordable medicines by examining the implementation of the product patent regime since 2005. The chapter is divided into five main components. The first component sets the context by describing the current domestic pharmaceutical industry market and the public health system in India. The second component describes the legal and policy framework surrounding drug regulation and data protection and the Patents Act. The third part looks at the interpretation of the patent laws by identifying patent litigation trends and analyzing key decisions on key provisions of the Patents Act. The fourth component examines the implementation of the product patent regime between 2005 and 2008 by reviewing a database of granted patents during the three-year period. The last component discusses the conclusions.

## **I. THE PHARMACEUTICAL INDUSTRY AND PUBLIC HEALTH SYSTEM IN INDIA**

### **I.1 The Pharmaceutical Industry in India**

The pharmaceutical industry in India is an important and steadily growing segment of the economy. The abolition of product patent protection for pharmaceuticals in 1972 and the introduction of a series of industrial and technological policies encouraged domestic production of medicines and facilitated research and development in India (Dhar and Rao, 2002). As a result, the Indian pharmaceutical industry was able to specialize in producing low cost generic medicines and has become a leading supplier of generic medicines in the world.

From being virtually non-existent in 1970 to dominating the domestic market at present, the Indian pharmaceutical industry has undergone a dramatic change in the last five decades (Sampath, 2005; Chaudhuri, 2010; Reddy, 2007; Dhar & Rao 2002). The growth of the Indian pharmaceutical industry has been attributed to four factors that were in place by the 1970s – (i) the enactment of the Patents Act, 1970, which abolished patent protection for pharmaceutical products, (ii) the establishment of national research institutions, (iii) setting up of government-owned pharmaceutical units to boost local production of drugs, and (iv) the initiative displayed by the private sector to take full advantage of the favourable policy environment (Reddy, 2007). These changes simultaneously created a disincentive for multinational pharmaceutical companies operating in India at the time and encouraged the growth of Indian companies.

The Indian government set up 12 public pharmaceutical companies across the country with the aim of producing local pharmaceuticals in the 1960s, with a special focus on antibiotics. The main strategy employed by the government was to import intermediates required for the manufacture of active pharmaceutical ingredients (or bulk drugs) so that the companies could conduct the last step of reverse engineering process within India to create local active pharmaceutical ingredients (Sampath, 2005). Although most of these public companies have today either closed down or become defunct, they facilitated the creation of a local pharmaceutical industry as they helped both in

technology absorption and manpower training (Reddy, 2007). As a result, the Indian pharmaceutical industry is now a highly profitable and advanced pharmaceutical industry in the world, specializing in high quality and low cost generic medicines (see box 1).

**Box 1**

**Overview of the Indian Pharmaceutical Industry**

The Indian pharmaceutical industry is ranked fourth globally in terms of volume (Episcom, 2010). The Indian pharmaceutical industry is a multibillion-dollar industry, currently valued at US\$ 17 billion, according to the Department of Chemicals & Fertilizers. It has been growing at the rate of 10 per cent annually, which is significantly more than the average rate of 7 per cent annual growth of the global pharmaceutical industry (KPMG, 2006). It is estimated that the Indian pharmaceutical industry would have tripled its growth from a market size of US\$6.3 billion in 2005 to about US\$20 billion by 2015 (McKinsey & Co., 2010).

There are more than 20,000 pharmaceutical units in India, most of which are small-scale businesses (KPMG, 2006). However, the market is dominated by around 250-300 medium to big size organized firms that account for 70 per cent of the market share; top ten companies account for 30 per cent of this (KPMG, 2006). The Indian pharmaceutical market is characterized by generic as well as patented products, with generic products dominating the market share. The share of Indian pharmaceutical companies in the domestic market has been steadily increasing. Since 2004, nine out of top ten pharmaceutical companies have been Indian. Indian companies dominate in the retail formulations market. Out of the top 20 pharmaceutical companies, 16 are Indian and only 4 are multinational (Chaudhuri, 2010).

**Exports**

The Indian pharmaceutical industry has seen rapid growth in exports. It is one of the biggest exporters of generic medicines in the world, ranking fourteenth (KPMG, 2006). Since the abolition of product patent protection for pharmaceuticals in 1972, exports

in pharmaceuticals have steadily grown, recently at an annual rate of 20 per cent (see figure 1). Indian companies export to both regulated markets such as US, Western Europe, Japan, Australia and New Zealand (with more elaborate regulatory requirements) and semi-regulated markets such as Asia, Africa, Eastern Europe and Latin America (with lower regulatory standards). The United States is the largest market for pharmaceutical exports from India, accounting for 23 per cent of formulations exports and 14 per cent of bulk drugs exports from India in 2007-2008 (Chaudhuri, 2010). The other top export markets for Indian pharmaceuticals include United Kingdom, Germany, Russia, South Africa and Brazil (DGCIS, 2010). The top five Indian pharmaceutical companies based on exports include Ranbaxy, Cipla, Dr. Reddy's, Aurobindo and Lupin (Cygnus Economics and Research, 2006).

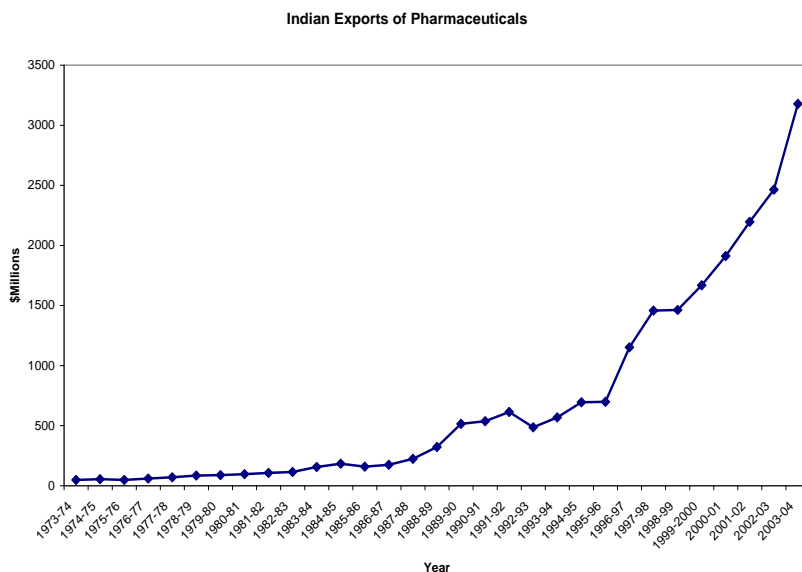
Table 1  
**Top 20 pharmaceutical companies in India**

CMIE companies	CMIE rank	CMIE net sales, INR Million, 2007-2008
Cipla Ltd.	1	41996.4
Ranbaxy Laboratories Ltd.	2	40799.6
Dr. Reddy's Laboratories Ltd.	3	37822.9
Lupin Ltd.	4	25706
Sun Pharmaceuticals Inds. Ltd.	5	23032.4
Aurobindo Pharma Ltd.	6	22718.9
Jubilant Organosys Ltd.	7	20013
Piramal Healthcare Ltd.	8	18989.9
Cadila Healthcare Ltd.	9	17154
Glaxosmithkline Pharmaceuticals Ltd.	10	16232.8
Glenmark Pharmaceuticals Ltd.	11	13466
Orchid Chemicals & Pharmaceuticals Ltd.	12	12376.4
Wockhardt Ltd.	13	11728
Ipca Laboratories Ltd.	14	10895.6



CMIE companies	CMIE rank	CMIE net sales, INR Million, 2007-2008
Divi's Laboratories Ltd.	15	10358.7
Torrent Pharmaceuticals Ltd.	16	9954.5
Alembic Ltd.	17	9907.2
Matrix Laboratories Ltd.	18	9510
Aventis Pharma Ltd.	19	9191.2
Biocon Ltd.	20	8782.4

Figure 1  
**Growth in Indian Exports of Pharmaceuticals**



Source: Park & Jayadev (2009).

### 1.1.1 *Innovation in the Pharmaceutical Industry*

As the primary purpose of building a local pharmaceutical industry was to encourage the local production of medicines at an affordable rate, the focus of the industry has been on incremental modification of existing

drugs, rather than developing new molecules or drugs. As such, the industry has acquired significant expertise in producing bulk drugs and formulations; with a number of pharmaceutical companies involved in developing novel drug delivery systems and novel combinations (Sampath, 2005; Reddy, 2007). Moreover, as a result of the large export market, the R&D focus of the largest Indian pharmaceutical companies has mainly been on developing generics (i.e. development of processes for manufacturing active pharmaceutical ingredients and development of formulations) to obtain marketing approvals for registration in foreign markets (Chaudhuri, 2010).

### New Drug Development

There has been some initiative on development of new drugs, by both public institutions as well as private pharmaceutical companies. The Central Drug Research Institute (CDRI) set up by the government of India under the Council of Science and Industrial Research (CSIR) has been leading in the development of new drugs. As of 2005, out of the 20 new drugs developed by public institutions, 10 were developed by CDRI (CDRI, Annual reports). However, the new drugs developed through public initiatives have not been so successful in the market. Only 6 out of the 20 new drugs were available in the market. The failure to successfully market the drugs has been attributed to the lack of commercial orientation of the public institutes as well as the failure to compete with similar products marketed by multinational companies (Chaudhuri, 2005).

In the private sector, pharmaceutical companies started investing in development of new chemical entities at the time of the TRIPS Agreement. Dr. Reddy's Laboratories, followed by Ranbaxy Laboratories first initiated R&D investments on new chemical entities. Eleven other pharmaceutical companies have followed suit since then. Notably, these companies are among the top spenders on pharmaceutical R&D and together spent 8.18 per cent of net sales on R&D in 2007/08. It is important to note that none of the companies engaged in development of new chemical entities have the capacity to carry out the entire process of drug development from start to finish. Instead, the model that they have adopted is to develop a new molecule to a certain stage and then license it to pharmaceutical companies in the developed

world, primarily multinationals, with the aim of generating revenue from licensing fees (Chaudhuri, 2010).

**Box 2**

**R&D Expenditure on Pharmaceuticals**

The share of government funded institutions on R&D expenditure is much less than that of the private pharmaceutical companies. In 1998-1999, out of the total estimated expenditure on pharmaceutical R&D in India, 63 per cent was contributed by the pharmaceutical industry and the remaining 37 per cent by publicly funded laboratories and institutions (Chaudhuri, 2005). There has been an increase in R&D spending in a segment of the pharmaceutical industry in recent years. In the early 1990s, R&D expenditures of the pharmaceutical industry amounted to only about 1.5 per cent of sales (Grace, 2004). However, since the 2000s, the R&D expenditure has considerably increased for some pharmaceutical companies. For example, for a group of 37 major spenders, the expenditure on R&D increased from 1.39 per cent of sales in 1992/93 to 3.89 per cent in 2001/02 and then sharply to 7.65 per cent in 2004/05 and 8.35 per cent in 2005/06 (Chaudhuri, 2010).

***1.1.2 Changes in the Pharmaceutical Industry: Post TRIPS***

The Indian pharmaceutical industry is undergoing a rapid change in the post TRIPS environment. As a result of the introduction of product patent protection for pharmaceuticals, there is an increased incentive to develop and market pharmaceutical products in India. According to estimate by McKinsey & Co., the share of patented products is likely to grow up to 10 per cent of the total pharmaceutical market by 2015 (McKinsey, 2010). This has encouraged multinational companies to renew their interest in India. Some multinational companies have established subsidiaries in India (such as Bristol Myers Squibb) and some others have made licensing agreements with Indian companies to market their products (Ernst & Young).

Another noticeable development is the acquisition of Indian companies by multinationals. In June 2008, one of India's largest pharmaceutical companies, Ranbaxy Laboratories, was bought by the Japanese multinational, Daiichi Sankyo. Three other Indian pharmaceuticals have also been acquired by multinationals – Matrix by Mylan, Shanta Biotechnics by Sanofi-Aventis and Dabur by Fresenius (Chaudhuri, 2010).

There is also a notable increase in the expansion of the retail formulations market. In order to respond to the post TRIPS product patent regime in the country, Indian pharmaceutical companies have started introducing and promoting new products in the market. The retail formulations market has grown at a fast and steady rate in the last three years, at around 14 per cent (Chaudhuri, 2010). According to data from ORG-IMS, one of the contributing factors in the growth of retail formulations market is the introduction of 'new' products, including new combinations of existing drugs or new formulation or composition (Chaudhuri, 2010). The number of products marketed by Cipla have increased manifold over the last two decades, from 92 in December 1994 to 803 in March 2008 (IMS Stockist Secondary Audit).

Furthermore, the huge export market for Indian pharmaceutical companies is also likely to change as most countries start implementing TRIPS requirements. A large percentage of exports are targeted for semi-regulated markets. However, as countries adopt stricter regulatory requirements, it might become more difficult to export to such markets.

## **I.2 The Public Health System in India**

India has the second largest population in the world with approximately 1.4 billion people (World Bank, 2008). Although it is one of the fastest growing economies in the world, it is still plagued with high rates of poverty, a huge disease burden and a fragmented health system. More than half of the entire population lives in poverty and approximately 42 per cent of the population lives on less than \$1.25 per day (UNDP, Human Development Report, 2009). Communicable diseases such as HIV, TB and malaria, as well as maternal and child health conditions account for nearly half the disease burden in India (NCMH, 2005).

Non-communicable diseases such as cardiovascular diseases, cancer and diabetes account for the other half of the disease burden and have been growing by the year (NCMH, 2005).

The Government of India's response to addressing health problems in the country has been weak. Government or public expenditure on health is a mere 1.2 per cent of the GDP, which is much lower than other developing countries. The majority of spending on health is paid for out-of-pocket, with the ratio of public to private expenditure on health at 1 to 3. There exists a public health infrastructure in both rural and urban areas. In the rural areas, the infrastructure is divided into a three-tier system – a sub-centre for every 5000 population, a primary health centre for every 30,000 population and a community health centre for every 100,000 population. In the urban areas, it consists of two levels – urban health centre for every 100,000 population and a general hospital. However, the existing public health infrastructure is not evenly distributed across the country; there is a shortage of staff, essential medicines and equipment in many public health care facilities. As a result of such inadequate facilities, a majority of the population does not seek or is unable to access public healthcare services (WHO, 2005).

Owing to the problems in the public healthcare system, most people rely on the private health sector, especially for outpatient services and doctor consultancies. This poses a huge burden on households on out-of-pocket expenditure, when a significant proportion of the population lives in poverty. As shown in table 2, household expenditure on health accounted for 72 per cent of the total health expenditure in India in 2001-2002. The World Health Organisation estimates that 60 per cent of the total out-of-pocket expenditure of households is spent on medicines (WHO, 2004).

The Ministry of Health and Family Welfare at the national level and the health ministries at the state level are responsible for framing health policies and implementing health programmes. The National Health Policy, formulated in 1984 envisages strengthening rural or primary level health systems to achieve better health outcomes. In 2005, the central government started the National Rural Health Mission that seeks to achieve universal access to healthcare services and prevention

and control of communicable and non-communicable diseases. In addition, there are several national health programmes addressing women and child health, HIV, TB, and malaria as well as other diseases. One important point to be noted is that government sponsored health programmes are heavily reliant on outside funding including the World Bank, foreign governments and other international funding agencies, raising questions about their sustainability (WHO, 2005).

Table 2

**Breakdown of Total Health Expenditure (THE) in India (2001-2002)**

<b>Source</b>	<b>Percentage of total health expenditure</b>	<b>Level in thousands</b>
<b>Public</b>		
State	12.6	132,709,065
Central	6.4	67,185,399
Local bodies	1.3	14,496,554
Sub Total	20.3	214,391,018
<b>Private</b>		
Households	72.0	760,939,107
Firms	5.3	55,365,142
NGOs	0.1	799,783
Sub Total	77.4	818,104,032
<b>External Support</b>		
Central	1.6	17,309,095
NGO	0.5	55,365,142
State	0.2	2,389,555
Sub Total	2.3	24,846,646
<b>Total</b>	<b>100.0</b>	<b>1,057,341,696</b>

*Source:* National Health Accounts (WHO, 2005).

## **II. POLICY AND LEGAL FRAMEWORK**

This section discusses the current policy and legal framework surrounding drug regulation and data protection as well as the patent system in order to gauge the changes taking place in the post TRIPS scenario.

## II.1 Overview of the Drug Regulatory System in India

The Drugs and Cosmetics Act, 1940 (“DCA”) is the principal Act that contains provisions for the registration, manufacture, marketing, distribution and import of drugs and cosmetics. The regulation of the pharmaceutical industry including licensing and quality control is carried out under the Drugs and Cosmetic Act, 1940.

Test data is regulated in India under the DCA and the rules thereunder, the broad purpose of which is to provide adequate controls and safeguards to the production (and eventual consumption) of these critical commodities. With respect to drugs, the DCA regulates every stage of the process: from import/manufacture, to distribution and eventual sale. The DCA is administered in India by the office of the Drugs Controller General of India (“DGCI”), through the Central Drugs Standard Control Organisation, a department of the Directorate General of Health Services under the Ministry of Health and Family Welfare.

Schedule Y of the DCA governs the process for application for approval to market (through manufacture or import) a new drug. It should be noted here that “new drug” as referred to in the DCA is significantly wider than the definition of New Chemical Entity (“NCE”) as referred to in Article 39.3 of TRIPS. Rule 122-E of the DCA defines the term “new drug” in much wider scope as:

*For the purposes of this part, new drug shall mean and include-*

*New substance of chemical, biological or biotechnological origin: in bulk or prepared dosage form, used for prevention, diagnosis or treatment of disease in man or animal which, except during local clinical trials, has not been used in the country to any significant extent and which, except during local clinical trials, has not been recognised in the country as effective and safe for the proposed claims.*

*A drug already approved by the licensing authority mentioned in Rule 21 for certain claims, which is now proposed to be marketed with modified or new claims, namely indications, dosage, dosage form (including sustained release dosage form) and route of administration.*

*A fixed dose combination of two or more drugs, individually approved earlier for certain claims, which are now proposed to be combined for the first time in a fixed ratio, or if the ratio of ingredients in an already marketed combination is proposed to be changed, with certain claims, viz., indications, dosage, dosage form (including sustained release dosage form) and route of administration.*

*Explanation: For the purpose of this Rule –*

*All vaccines shall be new drugs unless certified otherwise by the Licensing Authority under Rule 21:*

*A new drug shall continue to be considered as new drug for a period of four years from the date of its first approval or its inclusion in the Indian Pharmacopeia, whichever is earlier.*

Drugs and Cosmetics Rules, 122-E

Schedule Y of the DCA also sets out the types of test data to be submitted for marketing approval of a drug, depending on the situation with prior approvals for that drug. In theory, the DCA requires all clinical test data if the drug under consideration has never been approved before, in any other sovereign jurisdiction the world over. If prior approval has been granted, then a reduced data set – confirmatory clinical trials or Phase III data – is required. For subsequent approvals on an already approved drug that come within four years of the first approval – for generic manufacture, imports, etc. – only bio-equivalence and/or bio-availability studies are required. For subsequent approvals on an already approved drug that come after four years from the first approval, no studies are required to be submitted, and the applicant can receive approval directly through individual state drug licensing authorities. In addition to these procedures, the DGCI has the explicit powers under Schedule Y to waive all test data submissions altogether:

*For drugs indicated in life threatening/serious diseases or diseases of special relevance to the Indian health scenario, the toxicological and clinical data requirements may be abbreviated, deferred or omitted, as deemed appropriate by the Licensing Authority.*

Drugs & Cosmetics Rules, Schedule Y

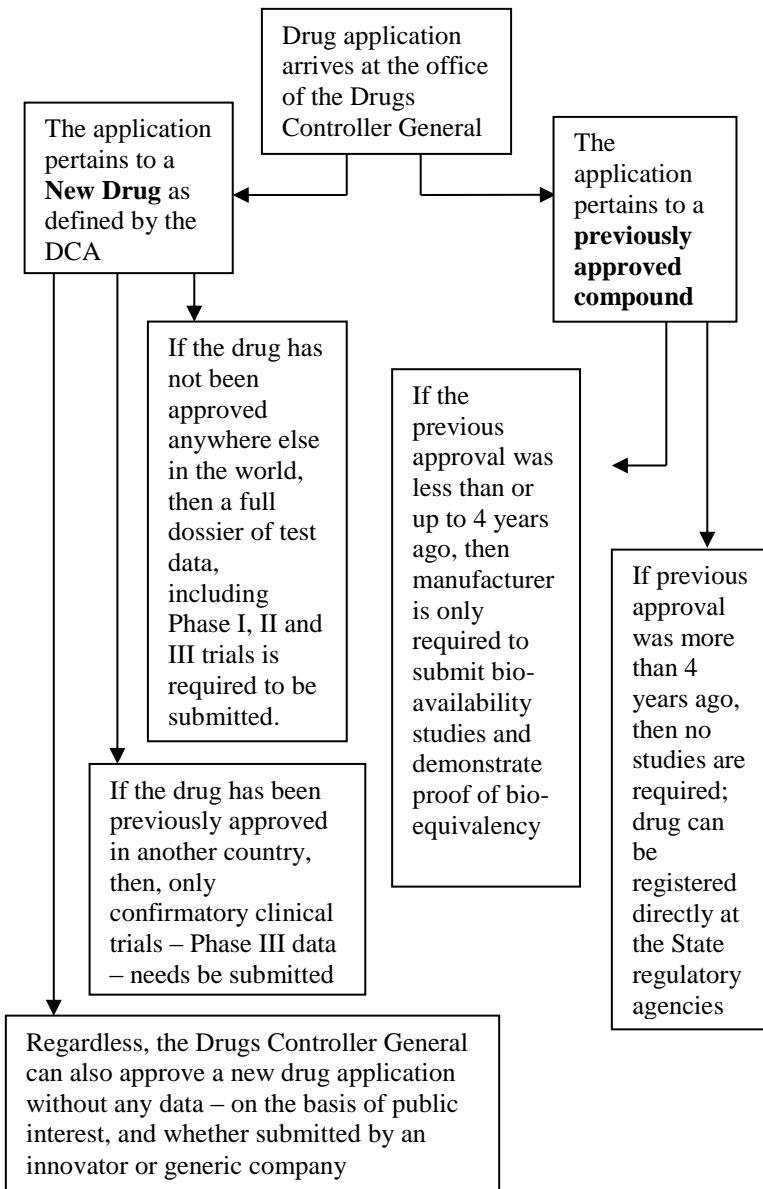


Thus, this provision allows the DCGI to permit a partial submission of clinical data (or to waive the requirement altogether) in cases where the medicine is of special significance to the Indian context. As such, it is not uncommon in India to have the generic version of a medicine introduced prior to the registration of the originator product (see figure 2).

## **II.2 Drug Pricing Policies**

To ensure the availability of drugs at affordable prices, the government enacted the Drug Price Control Order (DPCO) in 1970 under the Essential Commodities Act, 1955, which immediately brought almost all drugs in the market under price control. Since then, prices of drugs are regulated through DPCO under which the Central Government of India has the power to fix the maximum sale price for bulk drugs and retail formulations. DPCO has been revised several times since 1970. Over time, the number of drugs under price control has considerably reduced. The 1979 DPCO reduced the number of drugs under price control to 349, which was further reduced to 174 by a new DPCO of 1986. There are currently only 74 bulk drugs and their formulations under price control, covering 40 per cent of the pharmaceutical market (DPCO, 1995). The government formulated the National Pharmaceutical Policy in 2002 that among other things, proposed to further reduce the number of drugs under price control to 28. However, the government was unable to implement this proposal as the policy was challenged in court by a non-governmental organization that alleged that it was the responsibility of the government to ensure that essential and life-saving drugs were available at reasonable prices.

Figure 2 – Drug approval process in India



### **II.3 Patent Law in India**

The Patents Act of 1970 was based largely on the recommendations of a comprehensive review of India's patent system prepared by a committee headed by the jurist Rajagopala Ayyangar in 1959. Prior to the Patent Act that came into force in 1972, the Indian patent system was inherited from the British, which provided for a strong patent protection including product patent protection.

One of the main observations of the Ayyangar Report was that strong patent protection had failed to stimulate new inventions and did not necessarily encourage development of new inventions for industrial purposes that could benefit the country (Ayyangar, 1959). Concerned with the need to ensure access to affordable medicines, the Ayyangar Report recommended that the Indian patent law not recognize product patent protection for food and drugs in order to ensure availability of food products and medicines at a reasonable price. Ayyangar's main argument in support of this recommendation was that laws should be designed keeping in mind the economic conditions, state of scientific and technological advance and future needs of a country so as to minimize the abuse that can result from a patent monopoly system.

Based on the recommendations of the Ayyangar Report, the Patent Act, 1970 allowed for only process patent protection for claims relating to pharmaceuticals. Furthermore, the term for these process patents was shortened to five years from the date of granting and seven years from the date of filing. Another important provision of the patent act included automatic 'licenses of rights' made available three years after the grant of the patent on terms agreed upon by the parties or, failing agreement, terms set out by the patent controller (Patents Act, 1970, sections 87, 88). These provisions effectively lifted any patent barriers on pharmaceuticals (Dhar and Rao, 2004).

The enabling policy environment and lack of patent protection on pharmaceuticals in India allowed generic manufacturing companies to make triple combination antiretrovirals, vital in the treatment of HIV, at very low costs. The global movement for HIV treatment took a dramatic turn, when Cipla, a leading Indian pharmaceutical company offered to provide a fixed dosed combination for the triple therapy

(stavudine+lamivudine+nevirapine) for US\$350 per patient/year. The originator company was charging more than US\$10,000 at that time (Chaudhuri, 2005). Cipla's announcement forced the originator company to lower its prices and with other generic companies entering the competition, the prices for ARVs have fallen sharply since. Indian generic companies account for supplying more than 85 per cent of all ARVs in the developing world (Waning et al, 2010) and have contributed significantly to the global scaling up of the HIV treatment. Moreover, India has also been the major exporter of life saving cancer and HIV medicines to countries like Brazil, Thailand and Malaysia, where they issued compulsory licenses on these medicines (Khor, 2009). These facts underscore the importance of the Indian pharmaceutical industry as a key player in global access to affordable medicines.

However, the ability of the Indian pharmaceutical companies to continue to supply affordable generic medicines may be affected in the post TRIPS developments. India amended its patent law in 2005 in compliance with TRIPS Agreement, and reintroduced product patent protection on pharmaceuticals. Civil society and Members of Parliament voiced grave concerns regarding the impact of amendments to the patent law on access to affordable medicines and public health (Park, 2010). As a result of the oppositions and concerns, the parliament introduced some unique provisions in order to safeguard public health and prevent frivolous patenting of pharmaceuticals (Patent Amendment Act, 2005, section 3). The amendments also lay down provisions on pre and post grant opposition to patent applications that have been utilized by public interest groups and Indian pharmaceutical companies to successfully prevent and revoke granting of product patents on a variety of important medicines. These provisions will be discussed in some detail later in the chapter.

### ***II.3.1 Patentability Criteria: Overview of Provisions Relating to Patentability of Pharmaceuticals***

Although the TRIPS Agreement lays down the three criteria for patentability in Article 27.1, that is, novelty, inventive step and industrial application, it leaves considerable flexibilities for countries to define these terms. India is one of the pioneering countries to utilize

flexibilities in the TRIPS Agreement to implement stricter patentability criteria, particularly, in the case of pharmaceuticals.

Firstly, the Patents Amendment Act substituted the existing definition of ‘inventive step’ for “a feature of an invention that involves technical advance as compared to the existing knowledge or having the economic significance or both and that makes the invention not obvious to a person skilled in the art”. The specific requirements of ‘technical advance’ or ‘economic significance’ as criteria for inventive step appear to be more stringent. However, it has been argued that the use of the word ‘or’ dilutes the criteria as it can determine inventive step on the basis of economic significance alone (Musungu and Oh, 2006).

Secondly, ‘new invention’ under the Patents Amendment Act is defined as “any invention or technology which has not been anticipated by publication in any document or used in the country or elsewhere in the world before the date of filing of patent application with complete specification, that is, the subject matter has not fallen in public domain or that it does not form part of the state of the art”. This definition appears to adopt the ‘absolute novelty’ standards that hold that an invention fails for lack of novelty if it has been previously disclosed anywhere in the world. However, Section 25 of the Act seems to apply “relative novelty” standards as one of the grounds of opposition when stating that the invention was “publically known or publically used in India before the priority date of that claim” (Basheer, 2005).

Furthermore, section 3 of the Patents Amendment Act, lays down 15 broad categories of knowledge that “are not inventions within the meaning of the Act”. Of particular relevance to pharmaceuticals are – section 3(d), 3(e) and 3(i). These provisions are discussed below.

#### New uses/new forms

Section 3 (d) of the Patents Act, 1970 states that “mere discovery of a new form of a known substance which does not result in the enhancement of the known efficacy of that substance or the mere discovery of any new property or new use of a known substance or of the mere use of a known process, machine or apparatus unless such known process results in a new product or employs at least one new reactant”, would not be inventions within the meaning of the Act. It

further provides an explanation stating “for the purpose of this clause, salts, esters, ethers, polymorphs, metabolites, pure form, particle size, isomers, mixtures of isomers, complexes, combinations and other derivatives of known substance shall be considered to be the same substance, unless they differ significantly in properties with regard to efficacy”.

This clause has three separate and independent exclusions to patentability: 1) the discovery of new form of a known substance; 2) the discovery of a new property or new use of a known substance; and 3) the use of a known process. This clause, in particular the new form and new use exclusions, can have far-reaching effects in preventing secondary patents from being granted, and hence stopping evergreening of patents.

#### New use of a known substance

It has been observed that many “new” drugs that are approved for human use are in fact not new. Patent laws in the US, Europe and other jurisdictions have allowed researchers to obtain patents for new use by drafting their claims as “the method of treating disease X by the use of drug Y,” or “the use of drug Y for the treatment of X” (Park, 2010). It has been argued that adopting the practice of patenting new use of a known product expands the scope of patent protection inconsistently with the novelty requirement and should be avoided by developing countries (Correa, 2007). Section 3(d) attempts to prevent patents for new use by excluding from patentability the discovery of “any new property or new use of a known substance”. However, whether this clause is able to prevent new use claims from being patented would largely depend on how robustly the patent offices interpret and implement this new exclusion. For instance, several granted patents in India have been identified that appear to be new use claims reformulated as composition claims in the form: “A composition comprising Y for use in treating X” (Park, 2010).

#### New form of a known substance

Pharmaceutical companies have been obtaining secondary patents by claiming new forms of known substances. One way of doing this is to make improvements in the existing drug. For instance, it is a routine practice to develop a pharmaceutically acceptable salt form of a given

compound (Bastin et al, 2000; Gould, 1986). However, these improvements even if useful do not lead to the conclusion that they are particularly inventive and hence, raise questions about their patentability. Obtaining secondary patents on new forms is a strategic practice employed by pharmaceutical companies to artificially extend the period of market exclusivity of their products. Section 3(d) aims to prevent such questionable patents by excluding “mere discovery of a new form of a known substance” from patentability unless it results in “a significant enhancement of the known efficacy of that substance”. However, it is left to the patent offices or the courts to interpret what exactly “efficacy” means and what evidence is sufficient to establish significant enhancement in efficacy. Depending on the criteria chosen by the patent offices, this clause could either serve as an effective protection against many forms of secondary patents or be rendered toothless in preventing potential patent abuse (Park and Jayadev, 2009).

#### Mere admixtures

Pharmaceutical patents covering the final composition or formulation of a finished product are one of the most common types of secondary patents. These would include, for instance, a patent that covers the composition of an active ingredient with a number of commonly used excipients, filler and binding agents. However, it has been observed that claimed inventions in the field of compositions or formulations are most likely to lack inventive step as the processes to prepare formulations or compositions are generally well known (Correa, 2007).

Section 3(e) of the Patents Act can potentially reduce the number of such compositions/formulations that are patented in India. Section 3(e) states that “a substance obtained by a mere admixture resulting only in the aggregation of the properties of the components thereof or a process for producing such a substance” is not considered an invention and hence is not patentable under the Act. According to the Draft Manual of Patent Practice and Procedure, in order to be patentable under section 3(e), a composition or formulation must demonstrate synergistic effect (Patent Office, 2010). However, it is important to note that this is in addition to patentability requirements of novelty, inventive step and industrial application.

### Methods of treatment

It is yet another common practice to draft claims around the novelty objection for a new use of a known substance, such as, “A method of treating disease X by administering compound Y,” to obtain secondary patent. However, Article 27.2 of the TRIPS Agreement expressly allows countries to exclude “diagnostic, therapeutic and surgical methods for the treatment of humans or animals.” Although patent laws in many jurisdictions contain provisions that exclude method of treatment claims from being patentable, many of these same jurisdictions allow a further exception to this exclusion by providing that products for use in such methods do not fall under this exclusion. Thus, these jurisdictions expressly allow for method or use claims relating to treatment using medicinal products. It is to be noted that this exception is not a requirement under TRIPS (CIPR, 2004).

India, on the other hand, has provided an unusually broad exclusion for claims covering even the medicinal treatment of humans and animals. Section 3(i) of the Patents Act states that “any process for the medicinal, surgical, curative, prophylactic, diagnostic, therapeutic or other treatment of human beings or any process for a similar treatment of animals to render them free of disease to increase their economic value or that of their products” is not an invention under the Act. Hence, under the Indian patent law, any method or use claim that purported to utilize a medicinal product for the treatment of human beings would be excluded from patentability.

As indicated above, section 3 provisions of the Patent Act that relate to pharmaceuticals have the potential of safeguarding public health by preventing many of the secondary patents that are commonly granted. There is evidence to show that a large proportion of patents relating to medicines are secondary patents that potentially fall under one or more of the exclusions of section 3 of the Indian Patents Act (Park, 2010). If interpreted properly and applied rigorously, the safeguards in the Indian law can be very effective in removing many patent barriers that exist to generic competition. Many patent applications relating to important medicines have been rejected by the patent offices by applying the exclusions under section 3, although this has been done in most cases after third parties filed oppositions. It is yet to be seen how robustly the patent offices at their own instance apply



and interpret the public health safeguards under section 3 of the Act. A recent study conducted on implementation of the Indian patent law indicates that there is little evidence to show that section 3(d) has resulted in an overall reduction in the number of pharmaceutical patents granted in India, as compared to the European Patent Office (Sampath, 2010).

### **III. PATENT LITIGATION IN INDIA: OVERVIEW AND ANALYSIS OF KEY DECISIONS**

This section seeks to identify and analyse general trends in patent litigation relating to pharmaceuticals in India after the amendments to its patent law in 2005. In doing so, we attempt to find out whether pre and post grant opposition provisions have allowed and encouraged patent litigation in order to prevent secondary patents; and whether patent litigation is used as a tool by pharmaceutical companies, to block innovation or generic competition.

India has an on-going history of patent litigation relating to pharmaceuticals. Prior to 2005 and in the absence of product patent protection, the bulk of patent litigation related to infringement of process patents and exclusive marketing rights. However, with the change in the patent protection regime, there has been a surge in patent litigation relating to product patents. A significant contributing factor has been the introduction of pre and post grant opposition provisions (Patents Act, 1970, section 25). Indian pharmaceutical companies and civil society groups have used patent opposition provisions to target patent applications on important drugs.

Indian pharmaceutical companies such as Cipla, Ranbaxy, Torrents and Natco are among the top in filing patent oppositions. As of September 2010, a total of 14 patent oppositions filed by Cipla were decided by the patent office. A close second is Ranbaxy, which has had 12 of its patent oppositions decided by the patent office. In a majority of cases, patent oppositions have been successful in preventing the grant of the patent. Another interesting point to be noted is that a vast majority of the patent oppositions filed are at the pre-grant stage.

Most patent applications were rejected on the grounds of section 3(d). Products relating to diseases such as cancer drugs and HIV/AIDS appear to have been opposed the most. While most of the oppositions filed are against multinational companies, there are instances of Indian companies filing oppositions against each other as well. Taking advantage of the pre-grant opposition provisions that allow, ‘any person’ to file oppositions to patent applications, non-governmental organisations and civil society networks have been at the forefront of filing patent oppositions to key lifesaving drugs. The Cancer Patients Aid Association filed the first such case in opposition to Novartis’s application for the cancer drug imatinib. The Patent Office rejected the patent application on the grounds, *inter alia*, that it was a ‘new form of a known substance’ and hence not patentable under section 3(d). Following the success of imatinib opposition, a number of civil society organisations filed several oppositions on key drugs related to HIV/AIDS.

As a result of patent litigations including oppositions, a substantial body of case law that is emerging which could potentially provide valuable guidelines on how the courts and the patent offices should interpret the provisions of the Patent Act. Below is a brief description and analysis of some important court and patent office decisions.

### **III.1 Novartis v Union of India, Madras High Court**

Subsequent to the rejection by the Indian Patent Office of its patent application for imatinib, Novartis filed an appeal in the Madras High Court. In addition to appealing the rejection of the application itself, Novartis challenged the constitutional validity of section 3(d) as well as claimed that the provision was inconsistent with India’s obligations under WTO and the TRIPS Agreement. The Madras High Court dismissed the challenge and upheld the constitutional validity of section 3(d). In doing so, the Court noted:

“We have borne in mind the object which the Amending Act wanted to achieve namely, to prevent evergreening; to provide easy access to the citizens of this country to life saving drugs and to discharge their

Constitutional obligation of providing good health care to its citizens.”

Moreover, the Court also addressed the meaning of “efficacy” contained in section 3(d):

“The position therefore is, if the discovery of a new form of a known substance must be treated as an invention, then the patent applicant should show that the substance so discovered has a better therapeutic effect”.

Darland’s Medical Dictionary defines the expression “efficacy” in the field of pharmacology as “the ability of a drug to produce the desired therapeutic effect,” and “efficacy” is independent of potency of the drug. Dictionary meaning of “therapeutic” is the healing of disease - having a good effect on the body.” Going by the meaning for the word “efficacy” and “therapeutic” extracted above, what the patent applicant is expected to show is, how effective the new discovery made would be in healing a disease/having a good effect on the body.

In other words, the patent applicant is definitely aware as to what is the “therapeutic effect” of the [known substance] and what is the difference between the therapeutic effect of the [known substance] and the drug in respect of which patent is asked for. Therefore it is a simple exercise...for any patent applicant to place on record what is the therapeutic effect/efficacy of a known substance and what is the enhancement in that known efficacy.”

Thus, in defining “efficacy” in terms of “therapeutic efficacy” and distinguishing it from a drug’s potency, the Madras High Court, set a high threshold for meeting the efficacy requirements under section 3(d). This standard has been further explained and endorsed by the Intellectual Property Appellate Board (IPAB), which subsequently heard the appeal of the patent office’s rejection of Glivec.

### **III.2 Boehringer Ingelheim v Indian Network for People Living with HIV/AIDS (INP+) and Positive Women's Network (PWN), Delhi Patent Office**

Two civil society organisations, Indian Network for People Living with HIV/AIDS and the Positive Women's Network, filed an opposition against Boehringer Ingelheim's paediatric formulation of the ARV nevirapine. Thus, the Patent Office rejected the application and agreed with the opponents that it "should give a strict interpretation of patentability criteria as decision thereof shall affect the fate of people suffering from HIV/AIDS for want of essential medicine."

The opponents argued that the claims purported to cover the pharmaceutical composition containing nevirapine hemihydrate along with a number of inactive pharmaceutical components to produce a dosage form suitable for administration to children, and hence were excluded from patentability under both section 3(d) and section 3(e) of the Patent Act. The Patent Office, agreeing with the opponents concluded "the therapeutic effect of nevirapine, whether in hemihydrate form or anhydrous form, or whether administered in aqueous, tablet, parenteral or any other dosage form would remain unchanged. The applicant has failed to place on record any evidence to show that the therapeutic effect of nevirapine hemihydrate in aqueous solution is significantly enhanced over other known forms of nevirapine."

With regard to section 3(e)'s exclusion of "mere admixtures" the Patent Office further concluded that it agreed "with the opponent that the applicant failed to show either in the specification or through the submissions that the novel pharmaceutical composition claimed exhibits any of the properties above and beyond the aggregation of the constituent parts. So the claims fall under section 3(e) of the Act and are non-patentable."

### **III.3 Novartis v Torrent, Chennai Patent Office**

This decision of the Patent Office pertains to "new use of a known substance" which is excluded from patentability under section 3(d). The Novartis patent application claimed (among other things) the "use of

valsartan” “for producing a pharmaceutical preparation for the treatment” of various conditions, including lung and breast cancer. Initially when filed, Novartis had 15 claims including “use” claims and a number of composition claims.

After repeated objections from the patent office, Novartis narrowed its application to a single claim, as follows: “A pharmaceutical composition for the treatment of invasive lung cancer comprising a therapeutically effective amount of valsartan... or pharmaceutically acceptable salt thereof and comprising auxiliary microcrystalline cellulose.” Thus, all of the “use” claims were withdrawn by Novartis, and reformulated as a composition claim.

The Patent Office in rejecting the application concluded, “The said pharmaceutical composition comprises valsartan as active drug. There is no dispute that valsartan is known before the date of filing the present application... According to the Indian patent law, new use of a known substance is not patentable under Section 3(d). Since valsartan is the only ingredient in the said composition used to cure invasive lung cancer [but not microcrystalline cellulose, which has another purpose]... it appears that the sole aim of the applicant is to have [a] patent for the new use of valsartan.”

### **III.4 Roche v Cipla, Delhi High Court**

This judgment of the Delhi High Court is another landmark in affirming the legitimacy of public health considerations when interpreting the Indian patent law. The case related to a suit filed by the multinational pharmaceutical company Roche against the Indian generic company Cipla for infringing its patent on erlotinib, an approved drug for the treatment of lung cancer. Cipla filed a counterclaim against Roche alleging that the patent was invalid under the Indian patent law. Pending the final decision on the underlying patent dispute, Roche sought to get an interim injunction to prevent Cipla from manufacturing the generic version of the patented drug.

The Delhi High Court denied Roche’s application for interim injunction taking into consideration the public interest, including the

fundamental right to life guaranteed by Article 21 of the Constitution of India. In doing so, the Court observed: “The degree of harm [if an injunction is granted] is absolute; the chances of improvement of life expectancy; even chances of recovery in some cases would be snuffed out altogether, if injunction were granted. Such injuries to third parties are un-compensatable. Another way of viewing it is that if the injunction in the case of a lifesaving drug were to be granted, the Court would in effect be stifling Article 21 so far as those would have or could have access to Erlotcip are concerned.”

This decision of the Delhi High Court is pending in appeal at the Supreme Court of India. However, the Court’s reasoning, if upheld, could potentially pave way for the development of a form of jurisprudence that allows for what are essentially judicially-created compulsory licenses (Park and Jayadev, 2009).

As the above analysis indicates, Indian patent offices and courts have developed powerful precedents on interpreting the patent law, in particular, patent exclusion provisions that were introduced as public health safeguards at the time of the amendments. The civil society has actively utilized the provisions of patent opposition to advocate for access to medicines and the right to health.

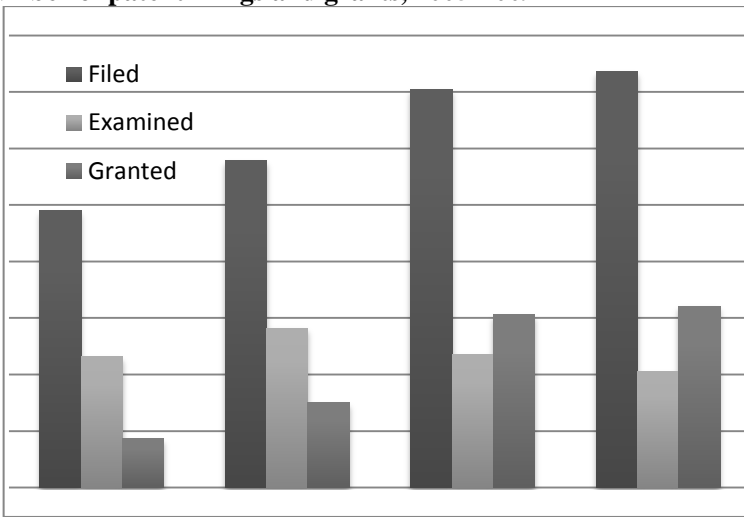
#### **IV. IMPLEMENTATION OF THE INDIAN PATENT LAW: ANALYSIS OF GRANTED PATENTS**

As discussed in previous sections of this chapter, the patent system and the policy environment have gone through a significant change since the patent law was amended in 2005. Some of the patent offices as well as court decisions provide powerful guidelines on interpreting Indian patent law provisions relating to pharmaceutical patents. However, it is not clear how consistently the principles laid out in the decisions of patent offices and courts are applied across all patent offices. The number of patents filed as well as granted is increasing every year (see figure 3). According to the latest list of pharmaceutical patents published by the patent office, a total of 3488 product patents on pharmaceuticals have been granted by the patent offices, between the

periods 2005-2006 and 2009-2010. The patent offices, with limited resources, deal with tens of thousands of applications every year. In order to identify the trends involved in granting patents and to gauge how often the public health safeguard provisions are applied while granting or rejecting patents, a review of granted patents between the periods 2005-2008 was conducted.

Figure 3

**Number of patent filings and grants, 2005-2009**



**IV.1 Methodology**

The period chosen for the review of granted patents was 2005-2008 so as to give a three-year window to understand the trends of granting pharmaceutical patents after product patent protection was introduced in 2005. All data collected was obtained from the information available in the public domain, published by the Indian Patent Office.

The data on granted patents was extracted from the information published by the Indian Patent Office in the database of granted patents. The five international classifications that are most commonly used to characterize drugs were used. These include A61K (“Human necessities;

Medical or Veterinary Science; Hygiene Preparations for Medical, Dental, or Toilet purposes"); CO7D ("Heterocyclic Compounds"); CO8 (Macromolecular Compounds); B82B (Nanostructures; Manufacture or treatment thereof) and C12P (Fermentation or enzymes processes to separate isomers). On classifications A61K and CO7D, 4250 patents were obtained with the assistance of Bhaven Sampat, of Columbia University, who was able to extract the information regarding granted patents from the Indian Patent Office website. Patents for the rest of the three classifications were manually downloaded from the database of granted patents on the patent office website. A total of 2347 granted patents from these five categories were further identified as relating to pharmaceuticals.

These 2347 granted patents were further codified into a database using variables such as country, patent number, date of filing, date of issue, date of expiry, international classification, title, first claim, name of the patent holder, country of the patent holder, INN, therapeutic class, type of claim (process, product, product and process, product and Markush, process and Markush) and further classification under secondary claims (salts, esters, ethers, polymorphs, isomer, pure form, metabolite, complex, isomer mix, combination, composition, formulation, other derivatives, therapeutic indication, active ingredient, dose). These variables were then used to further analyse the database.

Since all the data obtained was from the information available in the public domain, there are certain limitations to the methodology employed. Although the information available from the patent office website has markedly improved in the last couple of years, it is still not completely accurate. We encountered several errors in the data provided in the abstracts and complete specifications. In order to identify patents relating to pharmaceuticals, we relied on the information in the abstract and complete specifications. For those patents where it was not immediately clear from the abstract whether the patent related to pharmaceuticals, we relied on further information from the specifications. However, there were several instances when complete specification was not available. There were instances where the specifications did not have complete information; for example, the first claim or all claims were missing from many specifications.



This posed a considerable difficulty in coding the information under different variables.

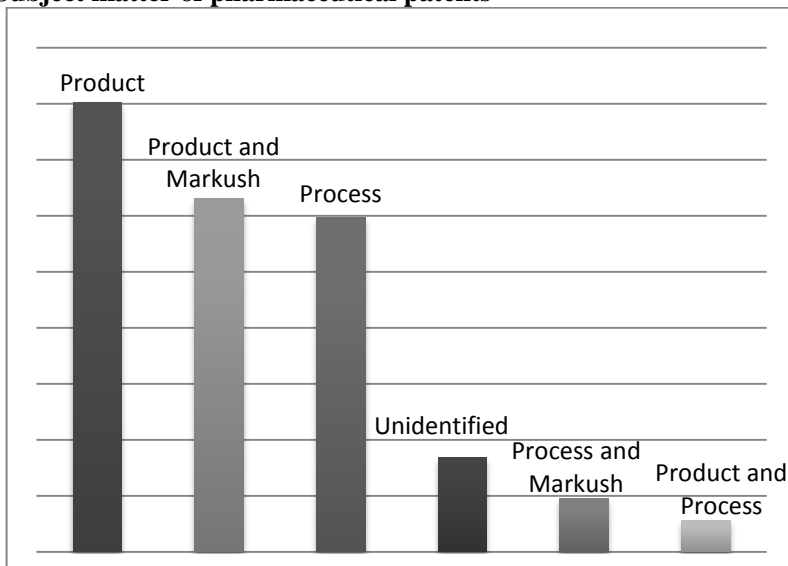
In addition to the above database, we further identified selected antiretroviral and anti-cancer drugs for which patents have been granted in India for a detailed analysis. These drugs were not identified using the database.

## **IV.2 Results and Discussion**

In all, a total of 2347 granted patents were identified as relating to pharmaceuticals. The majority of patents were product patents. Out of the 2347 patents, 1432 were product patents with 630 patents containing Markush claims. 168 patents could not be identified according to type due to the missing or incomplete information available (see figure 4).

One important point to be noted here is the increasing number of patents containing Markush claims. Markush claims often cover a family of a large number of compounds and maybe used to obtain a wide patent coverage over a large number of compounds whose properties have often not been tested. Thus, Markush claims generate exclusive rights over a broad set of compounds without prior testing or experimentation (Correa, 2007). In addition to raising concerns about their patentability, Markush claims, in particular, raise issues concerning disclosure and transparency. They pose a significant difficulty for identifying patent applications for opposition, since it is virtually impossible to make prior art searches for thousands or millions of compounds. It has been recommended that Markush type claims covering a large number of compounds should not be allowed; limiting the patent coverage to what is actually enabled by the disclosure in the patent specification (Correa, 2007).

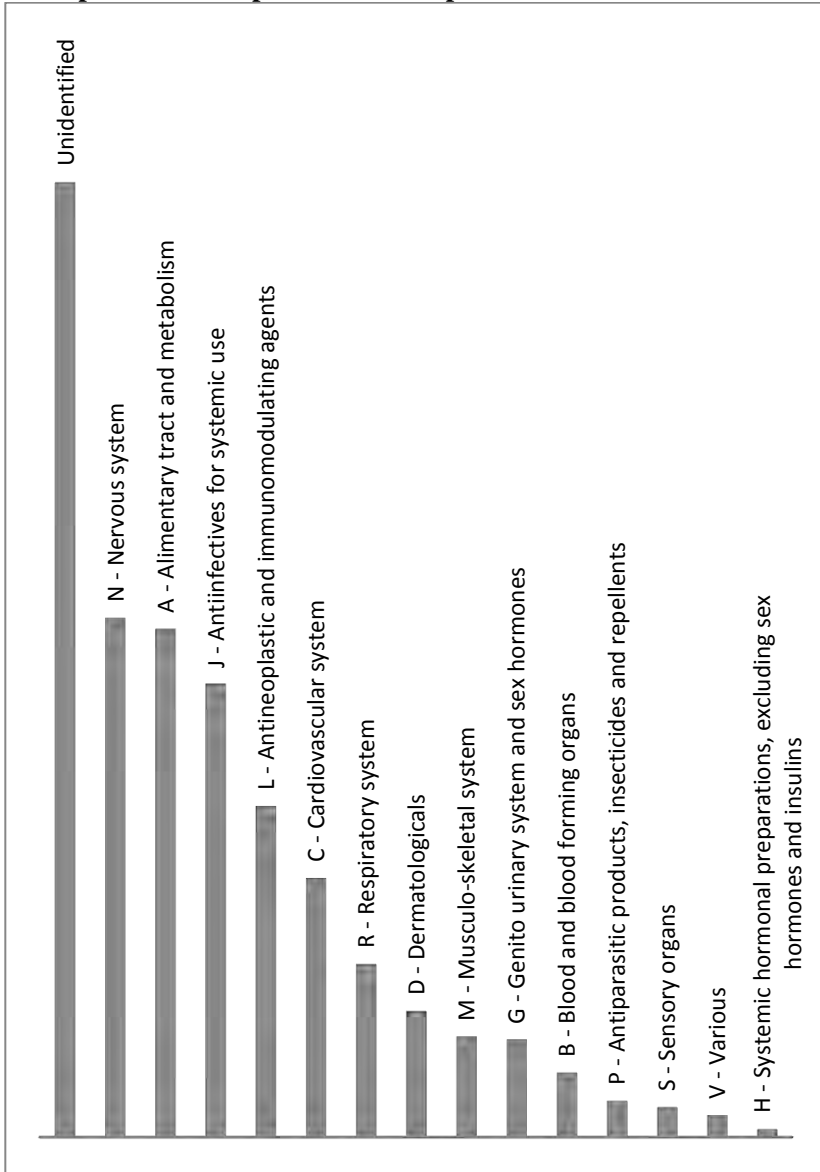
Figure 4  
**Subject matter of pharmaceutical patents**



The largest number of patents granted belongs to the therapeutic class ‘nervous system’ (a total of 331) closely followed by the therapeutic class ‘Alimentary tract and metabolism’ (a total of 324). It is important to note that as many as 609 patents could not be identified according to therapeutic class due to lack of relevant information, for instance, if the complete specification was missing and therapeutic class could not be determined from the abstract. In some cases, it was difficult to determine the therapeutic class if the patent had a Markush claim (see figure 5).

Figure 5

**Therapeutic class of pharmaceutical patents**



Of the countries of origin of the patent holder, India emerged with the largest number of patents closely followed by the United States (see table 3). Of the total number of patents granted to patent holders of Indian origin, most of the patents were process patents (333 out of 588). Table 4 gives a further breakdown of Indian pharmaceutical companies with number and type of patents granted. Patents belonging to patent holders from United States had a larger share of product patents (210 out of 455) with a substantial number of Markush patents.

Table 3

**Country of origin of patentees**

<b>Country of patent holder</b>	<b>Number of patents</b>
India	588
USA	455
Germany	238
Switzerland	184
Japan	132
United Kingdom	125
France	100
Sweden	74
Netherlands	46
Denmark	42
Belgium	33
Italy	30
Spain	21
Korea, Republic of	20
Israel	16
China	14
Argentina	2
Brazil	2
Cuba	2
Not Available	164

Table 4

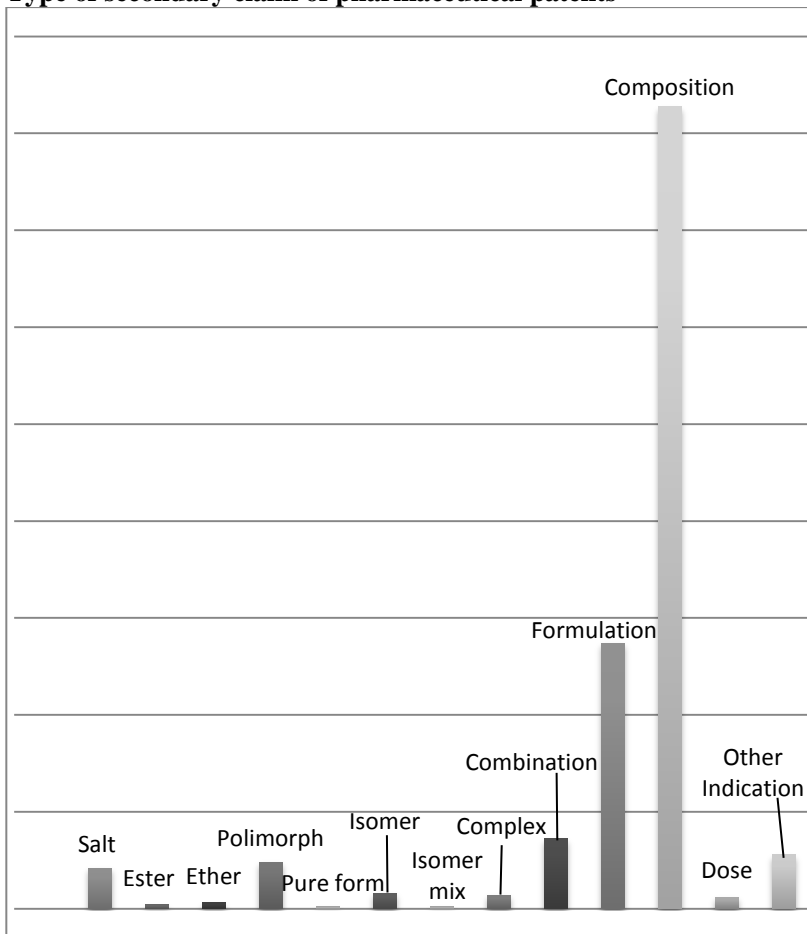
**Breakdown of Indian pharmaceutical companies and types of patents granted**

Patent holder company	Number of patents	Type of patent				
		Product	Product and Markush	Process	Process and Markush	Product and Process
Council for Scientific and Industrial Research	29	6	1	18	2	1
Hetero Chemicals Ltd.	22			22		
Orchid Chemicals Ltd.	22			16	5	1
Dr. Reddy's Laboratories Ltd.	17		9	7	1	
Natco Ltd.	17	4		11	1	1
Cadila Healthcare Ltd.	15	5	1	7	2	
Matrix Laboratories Ltd.	13			13		
USV Ltd.	13	5		7	1	
Sun Pharmaceuticals Ltd.	13	7		5	1	
Cipla Ltd.	12	6		4	1	1
Aurobindo Pharma Ltd.	12			12		
Lupin Ltd.	11	3	1	7		
Ranbaxy Laboratories Ltd.	10			10		

Moreover, the database results indicate that despite the patentability exclusions provided in section 3 of the Patent Act, a significant number of patents have been granted for questionable secondary claims. A total of 688 patents were identified as having secondary claims (see figure 6). Most of these claims were compositions (414) and formulations (137).

Figure 6

**Type of secondary claim of pharmaceutical patents**



Claims covering compositions and formulations are often claims for new use of a known substance or new form of a known substance that are not patentable under section 3(d). In addition, there was a significant number of claims covering salts, polymorphs and combinations that are also not patentable under section 3(d) as they are considered to be the same substance unless they differ significantly in properties with regard to efficacy. Moreover, a number of ‘method of treatment’ claims that are excluded from patentability under section 3(i) were also granted. These are covered under therapeutic indication category in the database.

### **IV.3 Analysis of Patents and Patent Applications Relating to ARVs and Cancer Drugs in India**

As the patents were being coded into the database, patents that appeared to relate to antiretroviral (ARV) medicines or cancer drugs were flagged as such. In addition, because the Indian Patent Office granted many of the patents relating to ARVs and cancer drugs after the study period (2008), additional research was conducted to determine which patents were granted on ARVs and cancer medicines after 2008. It should be noted that the patents identified below are limited to those drugs that have either already been granted regulatory approval, or are sufficiently late in development so as to have an INN. There were a large number of compound patents coded into the database that could **potentially** have use in AIDS or cancer treatment, but were not identified for further analysis as they could not be definitively linked with a known INN. The list of granted patents on ARVs and cancer drugs is displayed in table 5.

Table 5

#### **List of patents granted on ARVS and cancer drugs**

<b>INN</b>	<b>Patent No.</b>	<b>Patentee</b>	<b>Date of grant</b>	<b>Type of claims</b>	<b>Comments</b>
Abacavir (ARV)	219578	Medivir	27 Jun. 2008	Formulation; Method of use	Relates to combination of abacavir with alovudine (a compound abandoned in

<b>INN</b>	<b>Patent No.</b>	<b>Patentee</b>	<b>Date of grant</b>	<b>Type of claims</b>	<b>Comments</b>
					phase II trials)
Abacavir (ARV)	212734	Glaxo (GSK)	14 Dec. 2007	Formulation	Relates to liquid (paediatric) formulation of abacavir
Saquinavir (ARV)	200832	Roche	23 Feb. 2007	Formulation	Relates to formulation of saquinavir with mono-glyceride carrier
Ritonavir (ARV)	209151	Cristalia Produtos	17 Oct. 2008	Formulation	Relates to formulation of ritonavir in soft gel capsule
Nelfinavir (ARV)	222626	Roche	21 Nov. 2008	Formulation	Relates to formulation of nelfinavir in tablet form
Nelfinavir (ARV)	200223	Agouron	9 Feb. 2007	Process	Processes for producing nelfinavir
Rilpivirine (ARV)	222987	Janssen	12 Sep. 2008	Compound/Markush	New pyrimidine derivative compounds for HIV treatment
Raltegravir (ARV)	212400	Instituto di Ricerche di Biologia Molecolare	15 Feb. 2008	Compound/Markush	New compounds for inhibiting HIV integrase enzyme



<b>INN</b>	<b>Patent No.</b>	<b>Patentee</b>	<b>Date of grant</b>	<b>Type of claims</b>	<b>Comments</b>
Etravirine (ARV)	204028	Janssen	25 May 2007	Compound/Markush	New pyrimidine derivative compounds for HIV treatment
Maraviroc (ARV)	204132	Pfizer	31 Dec. 2010	N/A	Complete specification missing
Nilotinib (cancer)	237430	Novartis	01 Jan. 2010	N/A	Complete specification missing
Dasatinib (cancer)	203937	BMS	18 May 2007	Compound/Markush	New tyrosine kinase inhibiting compounds
Sunitinib (cancer)	209251	Sugen (Pfizer)	05 Oct. 2007	Compound/Markush	New tyrosine kinase inhibiting compounds
Lapatinib (cancer)	221171	GSK	20 Jun. 2008	N/A	Complete specification missing
Lapatinib (cancer)	221017	GSK	13 Jun. 2008	N/A	Complete specification missing
Sorafenib (cancer)	215758	Bayer	28 Mar. 2008	Compound/Markush	New Raf kinase inhibiting compounds
Erlotinib (cancer)	196774	Sugen (Pfizer)	05 Oct. 2007	Compound/Markush	New tyrosine kinase inhibiting compounds

In addition, because of the liberal opposition procedures in Indian patent law, as well as the stringent requirements of patentability as laid out in the Patents Act, there were a large number of patent applications relating to ARVs and cancer medicines that were rejected

by the Indian Patent Office. These patent applications are laid out in table 6.

Table 6

**List of patent applications on ARVs and cancer drugs rejected**

INN	Application number	Applicant	Opposed	Type of claims	Comments
Darunavir (ARV)	329/DEL/2004	Tibotec	Yes	Process	Rejected as lacking inventive step; not an invention under 3(d)
Darunavir (ARV)	3598/DELNP/2004	Tibotec	Yes	Pseudo-polymorph of Darunavir	Rejected for lack of inventive step; not an invention under 3(d) and for insufficient disclosure
Darunavir/ritonavir (ARV)	1647/DELNP/2000	Tibotec	Yes	Combination	Rejected for lack of inventive step
Erlotinib (cancer)	IN/PCT/2002/507/DEL	OSI	Yes	Polymorph/Process for preparing polymorph	Polymorph claims rejected under 3(d)
Gefitinib (cancer)	2488/DELNP/2004	Astra Zeneca	No	Crystalline form	Product claims rejected under 3(d)
Gefitinib (cancer)	841/DEL/1996	Astra Zeneca	Yes	Compound/Markush	Rejected for lack of novelty, inventive step and 3(d)

<b>INN</b>	<b>Application number</b>	<b>Applicant</b>	<b>Opposed</b>	<b>Type of claims</b>	<b>Comments</b>
Imatinib (cancer)	799/CHE/2004	Novartis	Yes	Polymorph	Rejected for lack of inventive step; not an invention under 3(d) and for insufficient disclosure
Imatinib (cancer)	1602/MAS/1998	Novartis	Yes	Polymorph	Rejected for lack of novelty, inventive step; not an invention under 3(d) and for insufficient disclosure
Lopinavir/ritonavir (ARV)	339/MUMNP/2006	Abbott	Yes	Formulation	Rejected for lack of novelty, inventive step; not an invention under 3(d) and 3(e)
Nevirapine (ARV)	2485/DEL/1998	Boehringer Ingelheim	Yes	Formulation	Rejected for lack of inventive step; not an invention under 3(d) and 3(e)
Tenofovir (ARV)	896/DEL/2002	Gilead	Yes	Fumarate salt	Rejected for lack of inventive step; not an invention

INN	Application number	Applicant	Opposed	Type of claims	Comments
					under 3(d)
Tenofovir (ARV)	2076/DEL/1997	Gilead	Yes	Ester prodrug	Rejected for lack of inventive step; not an invention under 3(d)
Tenofovir/Emtricitabine (ARV)	3383/DELNP/2005	Gilead	Yes	Combination	Rejected for lack of inventive step; not an invention under 3(d) and 3(e)

A few observations can be made from the tables above. First, from those patents for which the complete specifications were available, the majority of the granted patents (6 of 11, or 55 per cent) are those relating to the active compound itself, and not to secondary features of the medicines. Because these compound claims are generally formulated as broad Markush claims, some or all of these patents may be subject to the objection, as described by Correa (2007), that the thousands (if not millions) of possible compounds covered by these claims are insufficiently described and enabled. However, as a general matter, claims covering a new compound (or a class of compounds) would presumably be less susceptible to the well-known objections that are levied against the various types of secondary patent claims, and which are, to a large extent, made potentially unpatentable in Indian law.

Second, all but one (12 of 13, or 92 per cent) of the patent applications on ARVs and cancer medicines that were rejected by the Indian Patent Office were the subject matter of pre-grant oppositions filed. The sole exception, AstraZeneca's application (2488/DELNP/2004) relating to a crystalline form of the cancer drug gefitinib, was unopposed but partially rejected, but the process claims were allowed to proceed.

Third, the subject matter of all but two (11 of 13, or 85 per cent) of the patent applications on ARVs and cancer medicines that were rejected related to the typical secondary patents that the various features of Indian patent law were enacted to prevent. Five applications related to polymorphic or other crystalline forms of a known drug; two related to a combination of two known drugs; two related to a specific formulation of a known drug; and two related to either a salt or ester prodrug of a known substance.

Remarkably, section 3(d), often commonly understood to be applicable generally to new forms of known substances such as salts, polymorphs and the like, was used as the basis for rejecting a series of compound claims covering the cancer drug gelfitinib (841/DEL/1996). Whether or not Indian jurisprudence surrounding the scope of section 3(d) will develop so as to render structurally analogous but distinct molecules potentially unpatentable is not known, but potentially represents a vast expansion of section 3(d)'s currently understood scope.

Finally, of the six patents that were granted that did not cover the active compound, it is noteworthy that none of these patent applications were opposed during examination. With the exception of the paediatric formulation of abacavir, the list of granted secondary patents is remarkable in that they relate to compounds no longer recommended by the World Health Organization's ART Treatment guidelines (e.g., saquinavir, nelfinavir); relate to compounds that were abandoned during clinical trials (i.e., alovudine); or relate to formulations that are disfavoured (i.e., soft-gel capsules of ritonavir). It is entirely possible that these two observations are related; that due to the relatively smaller degree of public health significance of these patent applications, they were less likely to be opposed, and as a result, much more likely to be granted.

## V. CONCLUSIONS

Almost six years into the TRIPS mandated product patent regime, the Indian pharmaceutical industry still remains the leading supplier of quality generics and continues to grow at an excellent rate. However, as discussed in the chapter, there are significant changes taking place within the industry as it prepares itself to respond to the product patent market, with increased collaboration with multinational companies being one of the strategies employed by the Indian industry. There has been a significant increase in R&D spending among the top pharmaceutical companies in the past decade. However, the R&D focus of most pharmaceutical companies remains on developing generics and modifications of existing molecules. The initiatives of some companies to develop new molecule entities are yet to be successful. Moreover, none of the companies involved in new drug development are focusing on neglected diseases, prevalent in developing countries.

Instead, the focus of the pharmaceutical industry remains on exports and the local domestic market. The Indian pharmaceutical industry has a huge presence in the domestic market and is largely driven by demand in the private health care sector that accounts for 70 per cent of total expenditure on health in the country. Therefore changing income demographics and health care environment will contribute significantly to its growth. Factors such as rising disposable income, improvement in medical infrastructure and greater health insurance penetration are likely to account for the growth of the industry. As McKinsey & Co have pointed out, the growing prevalence of life-style diseases such as diabetes, coronary heart diseases, and obesity, will be a significant factor in spurring the growth of the pharmaceutical industry. As such, there is little incentive for the Indian pharmaceutical companies to increase their R&D focus on neglected diseases that affect the vast majority of people, especially the poor, in India and other developing countries.

In the context of legal and policy environment there are certain emerging issues that could have far reaching consequences for generic companies as well as access to affordable medicines. The Indian Government is considering amendments to the DCA and other relevant










legislations with regard to data protection in the context of its on-going negotiations on a free trade agreement with the European Union. If India accedes to the EU's demands for data exclusivity, the ability of the domestic pharmaceutical industry to provide affordable generic medicines could be severely hindered.

The Indian patent law contains provisions that could act as public health safeguards and protect against patent barriers to affordable generic production of medicines. However, the review of patents granted between 2005 and 2008 indicates that a significant number of secondary patents have been granted by the Indian Patent Office. This suggests that patent offices may not be applying and interpreting these provisions as robustly as required under the current law.

Moreover, where secondary patents have been rejected or revoked, it has been mostly at the instance of pre or post grant oppositions filed by civil society and generic companies. These oppositions have led to some landmark decisions and precedents by courts and patent offices that, if broadly adopted and upheld in subsequent judgments, could lead to India developing a uniquely progressive jurisprudence that expressly takes into account the public health ramifications of the decisions made at the patent office.

The Indian Patent Office has undergone a positive and significant change in the transparency of the information regarding pending and granted patents. The Indian Patent Office has now started publishing granted patents with complete specifications. It is also possible to search patent applications and granted patents through different search variables available. However, there remain many shortcomings in the information available. During this study, there were several instances where full and accurate information could not be obtained because of the gaps in the information in the patent office database.

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# **CHAPTER 6**

## **COUNTRY CASE STUDY: SOUTH AFRICA**

Yousuf Vawda

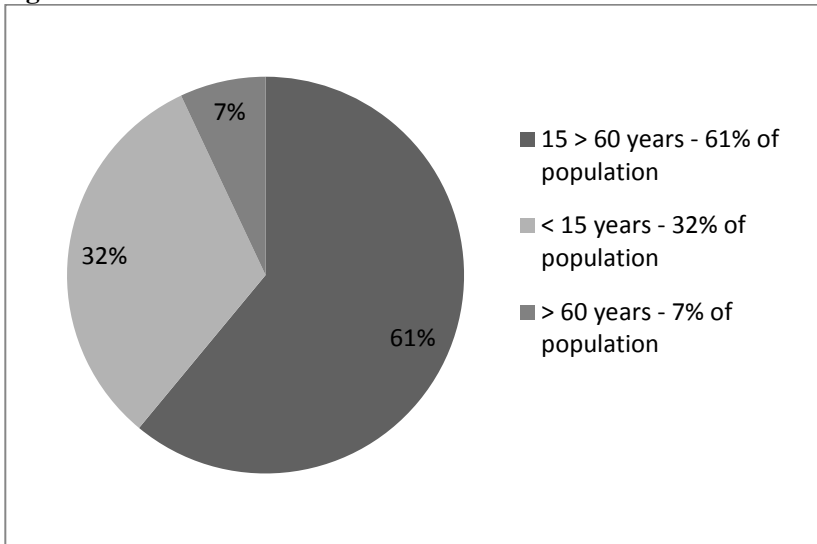
### **I. INTRODUCTION**

“The roots of a dysfunctional health system and the collision of the epidemics of communicable diseases in South Africa can be found in policies from periods of the country’s history, from colonial subjugation, apartheid dispossession to the post-apartheid period. Racial and gender discrimination, the migrant labour system, the destruction of family life, vast income inequalities, and extreme violence have all formed part of South Africa’s troubled past, and all have inexorably affected health and health services.” (Coovadia et al, 2009).

### **II. HEALTH AND MEDICINES REGIME**

South Africa is an upper middle-income country with an estimated population in mid-2010 of just under 50 million, with almost 80 per cent being black Africans. In the last Census (2001), 7.3 per cent of the population was aged 60 years or older, and 32.1 per cent was younger than 15 years. In 2008 the median age was 24 years. Between 2001 and 2010, the aging index (the number of people aged 65 and over per 100 youths under age 15) had increased from 11 to 16, but was nearly 70 in the white population. By contrast, the ageing index in 2008 was highest in Western Europe (113) and Eastern Europe (97), and lowest in Sub-Saharan Africa (7) and the Near East (14). (Day and Gray, 2010).

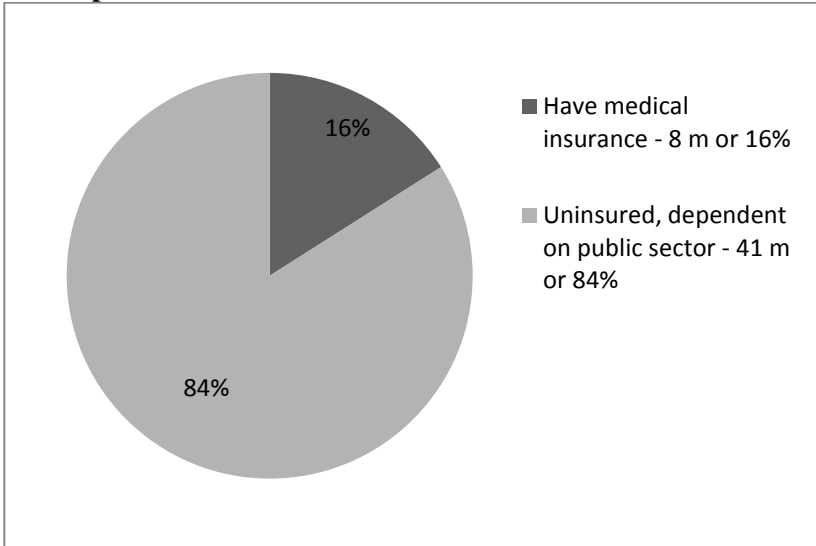
**Figure1**  
**Age distribution in South Africa**



*Source:* Adapted from Day & Gray, 2010.

According to this study, over 41 million South Africans did not have medical insurance in 2009, and were dependent on either the state or out-of-pocket payment for their health requirements. However, for those who are uninsured, all health services at primary health care facilities are free of charge, including medicines listed on the Essential Drugs List. In 2009, 74.4 per cent of the white population was insured, compared with only 9.0 per cent of the black African population. The uninsured generally access healthcare services at clinics, community health centres and hospitals operated by the provincial and local authorities, but may also purchase services and products out-of-pocket in the private sector. The insured population would generally access healthcare services from private health practitioners, pharmacies and private hospitals. Despite the vast majority of the population being uninsured, the majority of health professionals practise in the for-profit private sector.

Figure 2

**Health provision in South Africa**

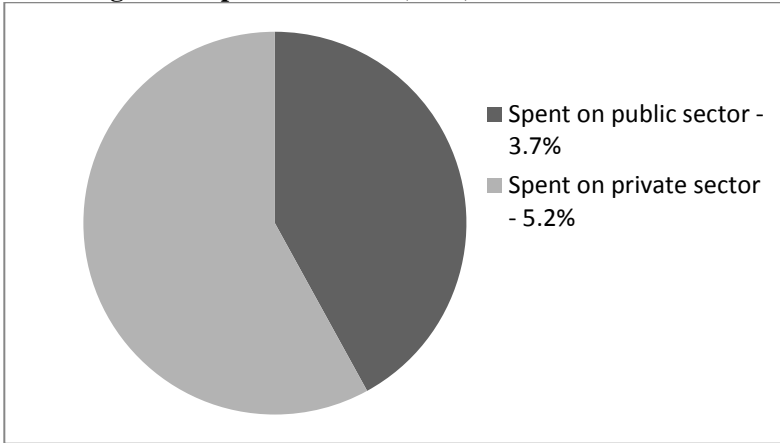
*Source:* Adapted from Day & Gray, 2010.

South Africa is confronted with ‘four concurrent epidemics’ - HIV and AIDS, other infectious diseases, violence and injuries, and non-communicable diseases. Despite its middle-income status, it has health outcomes, such as child mortality, that are worse than many poorer countries (Coovadia et al., 2009). As the population ages, the burden of non-communicable disease is expected to increase (Mayosi et al., 2009). However, the health problems that have received the greatest attention, and for which access to affordable quality medicines is imperative, are the linked epidemics of HIV and tuberculosis. South Africa has both the largest number of HIV-infected persons of any country and also the largest number on antiretroviral treatment (Abdool Karim et al., 2009).

In 2009, South Africa spent 8.9 per cent of Gross Domestic Product (GDP) on health, made up of 5.2 per cent expended in the private sector and 3.7 per cent in the public sector. The per capita expenditure was ZAR9605 (approximately \$1372) per medical scheme

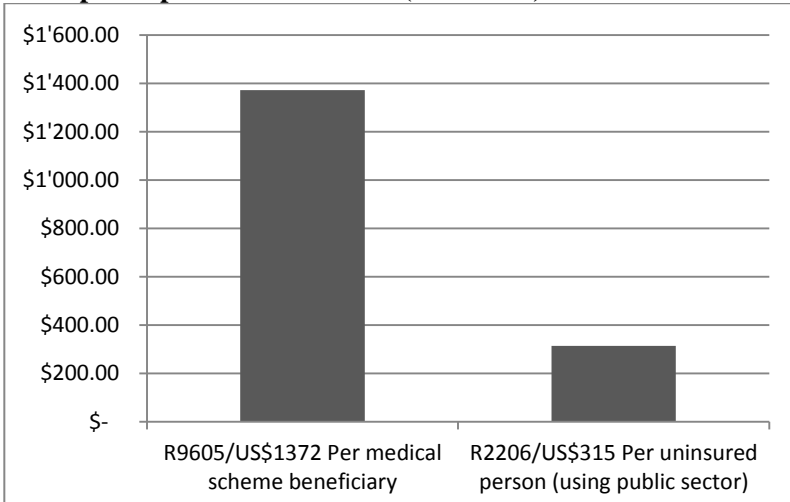
beneficiary in 2009, compared with ZAR2206 (\$315) per uninsured person in the 2009-2010 public sector fiscal year.

Figure 3  
**Percentage GDP spent on health (2009)**



Source: Adapted from Day & Gray, 2010.

Figure 4  
**Per capita expenditure on health (2009-2010)**



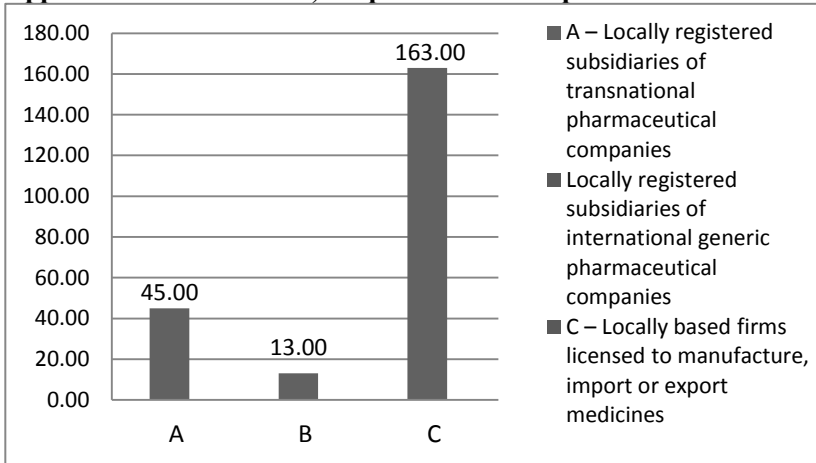
Source: Adapted from Day & Gray, 2010.

### III. PHARMACEUTICAL MARKET AND PRODUCTION

South Africa has a large and highly developed pharmaceutical system, including considerable local production capacity. In October 2009, the South African Medicines Control Council licensed 221 entities as manufacturers, importers, and exporters of medicines (or in at least one of these categories). Of these, 76 entities were listed as manufacturers of medicines, meaning that some element of local production was involved. Forty-five were locally-registered subsidiaries or offices of transnational pharmaceutical concerns, including the major American and European innovators in this field. While the majority of these were licensed as importers and exporters, some were licensed to manufacture locally and operated such plants. Thirteen of the remaining entities were locally-registered subsidiaries or offices of international generic pharmaceutical manufacturers, including Teva, Sandoz and Ranbaxy while 163 were locally-based firms licensed to manufacture, import or export medicines. This excluded those operating exclusively as wholesalers or distributors of medicines. The oldest South African generic manufacturers have been operating for over 100 years and are major players in the local market, if not globally (Gray and Vawda, 2011).

Figure 5

#### Approved manufacturers, importers and exporters of medicines



Source: Adapted from MCC, 2009.

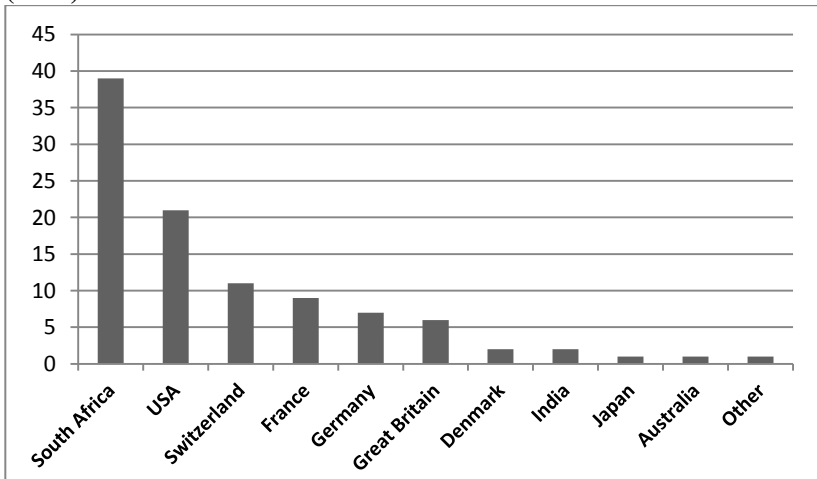


However, a 2005 report on the issue of local production cited that the pharmaceutical industry in South Africa was then “small and not very wealthy”, and lacking “an ability to achieve economies of scale in production” (Kaplan and Laing, 2005). As expected, local research and development has largely been restricted by formulation issues, although there are new drug discovery projects in a number of public-private partnerships and in academic research centres.

Nevertheless, South African companies feature prominently in terms of pharmaceutical market share. The most recent statistics indicate that South African companies command a significant slice (39 per cent) of the local market (IMS Health South Africa, 2011). This is followed by the USA with 21 per cent, Switzerland (11 per cent), France (9 per cent), Germany (7 per cent), Great Britain (6 per cent), Denmark and India (2 per cent each), and Japan and Australia (1 per cent each).

Figure 6

**Market share of pharmaceutical trade in South Africa by country (2010)**



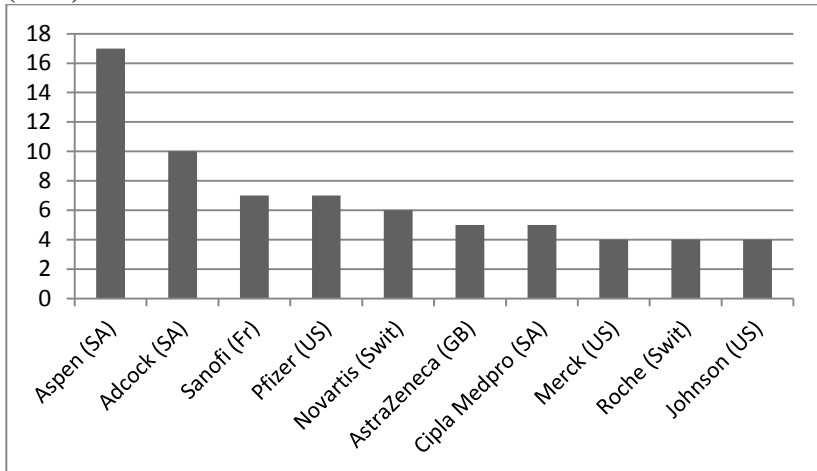
*Source:* Adapted from IMS Health South Africa, 2011.

Individually, two South African companies lead the supply of medicines in the country. Aspen Pharmacare commands 17 per cent of the local market, and Adcock Ingram follows with 10 per cent. The leading foreign companies are Sanofi-Aventis (France) and Pfizer

(USA), each with 7 per cent; Novartis (Switzerland) with 6 per cent, followed by AstraZeneca (Great Britain) and Cipla Medpro (South Africa), each with 5 per cent of market share. Others with a significant presence in the market are Merck (USA) with 4 per cent, Bayer (Germany) with 3 per cent, and Abbott (USA) and Lilly (USA), each with 2 per cent.

Figure 7

**Top 10 pharmaceutical companies in South Africa by market share (2010)**



Source: Adapted from IMS Health South Africa 2011.

#### IV. MEDICINES REGULATION

Medicines have to be registered by the Medicines Control Council (MCC), a statutory regulatory authority located within the national Department of Health (Gray, 2007). It is required to consider only issues of quality, efficacy and safety, and there is no linkage between patent status and regulatory approval. The Enabling Medicines and Related Substances Act, No 101 of 1965 also provides for a degree of regulation of medicine pricing, exercised by the Minister of Health, as informed by a Pricing Committee (Gray, 2009). The Minister issues an annual maximum limit to price increases for medicines sold in the private

sector. The dispensing fees charged by pharmacists and other licensed dispensers are also regulated, and adjusted on an annual basis.

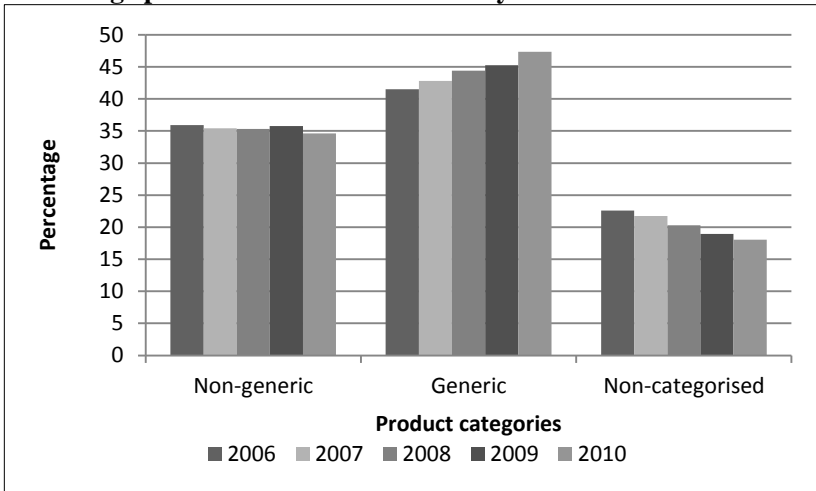
An international benchmarking system, in which the prices of innovator products will be compared with those in a basket of countries, has been proposed but not yet implemented. In the public sector, medicines are procured in terms of centrally determined competitive bidding (tender) processes, limited to locally-registered products, and these are predominantly generics although some branded products are used (IMS Health, 2009).

The 2010-2012 antiretroviral tender also introduced a benchmarking step, where indicative global best prices were provided before tenders were accepted. In this way, the public sector has been able to achieve competitive prices for first and second-line antiretrovirals. However, the prices of newly-launched patent-protected medicines, generally brought to the market by transnational innovator firms, remain unregulated. Such medicines may not easily be included in the public sector Essential Drugs List, and may be denied reimbursement or attract considerable co-payments in the private sector (Gray and Vawda, 2011).

Since 2003, South Africa has used a requirement for mandatory offer of generic substitution to promote the use of lower-cost generic medicines. The trends in private sector medicines sales over time are shown in figures 8 and 9. In this categorisation, non-generic products are those that are patent-protected, original brands sold after patent protection has lapsed and first-launch products without patent protection. Generic medicines constitute almost 50 per cent of the private sector market share by volume and 30 per cent by value. In the public sector, the limited Essential Drugs List contains predominantly older, off-patent medicines, and these are procured by tender, making substitution irrelevant.

Figure 8

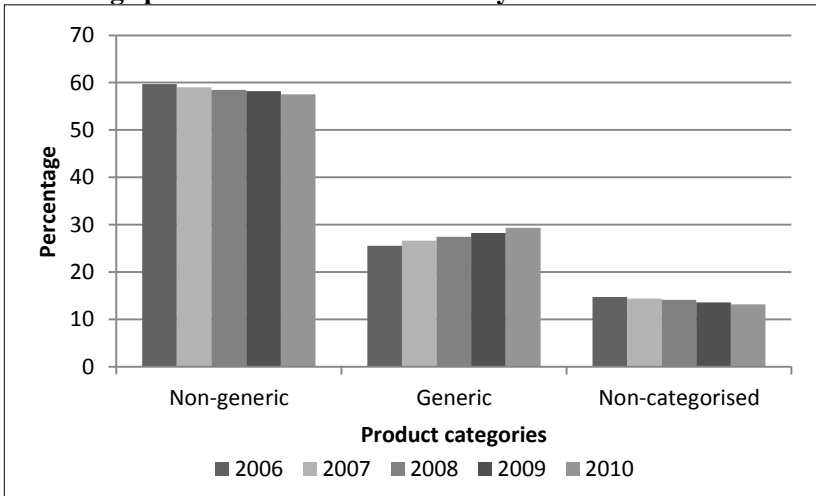
**Percentage private sector market share by volume**



Source: IMS Health South Africa, 2010.

Figure 9

**Percentage private sector market share by value**



Source: IMS Health South Africa, 2010.

## **V. INTELLECTUAL PROPERTY PROTECTION IN SOUTH AFRICA**

### **V.1 Background**

South Africa has had patent legislation since at least 1916, and the statute currently in force was promulgated in 1978 (Union of South Africa, 1916; Republic of South Africa, 1978). South Africa undertook to become TRIPS-compliant in 1997 (Republic of South Africa, 1997a), with the passage of the Intellectual Property Laws Amendment Act. South Africa also became bound by the Patent Co-operation Treaty in 1999 (Burrell, 1999). Further amendments to the Patent Act were made in 2002 and 2005 (Republic of South Africa, 2005; Republic of South Africa, 2002). While on the face of it, this appears to be a rational outcome of the process of patent harmonisation, it can also be viewed as further evidence of the extension of patent monopolies by simplifying the process of obtaining them in developing countries, and also of the process of negotiations which resulted in such agreements and treaties (Drahos and Braithwaite, 2004).

Compliance with the international intellectual property regime has come at a great cost. Many developing countries have adopted the new intellectual property regime against their own best interests, and out of fear of inviting trade sanctions if they did not. Countries such as South Africa and Brazil attracted the wrath of the US when they adopted legislation which, in the view of the latter, used flexibilities in the TRIPS Agreement more broadly than the US wanted (Abbott, 2002, Bond, 1999). The 1997 amendments to the South African Medicines Act drew not only a legal challenge (Pharmaceutical Manufacturers' Association and Others v President of the Republic of South Africa and Others, case no. 4183/98, High Court of South Africa, Transvaal Provincial Division), but also saw the US Trade Representative placing South Africa on its 301 Watch List, a precursor to sanctions. At about the same time, the US lodged a complaint with the WTO Dispute Resolution Panel against Brazil regarding its compulsory licensing legislation.

The South African case was withdrawn under intense international scrutiny, and the complaint against Brazil was also

withdrawn. However, such strong-armed tactics persist till present date in trade negotiations between the developed and developing countries. South Africa has recently engaged in negotiations on a free trade agreement (FTA) with the US, through its participation in the Southern African Customs Union, and although the formal FTA talks have stalled, there are on-going discussions on selected trade topics (Inside US Trade, 2006). As a result, many countries have adopted measures in their patent systems which go beyond those required by the TRIPS Agreement. An example of such measures is the heightened level of protection for clinical test data demanded by pharmaceutical manufacturers, which is not mandated by Article 39 of TRIPS, and which the US is routinely demanding be included in bilateral and regional trade negotiations.

South Africa's patent legislation already contains more stringent conditions than those required by international law (Republic of South Africa, 1978). Examples include the disclosure standards (section 32) and the process for compulsory licensing (section 56). Furthermore, it has not fully utilised provisions in its existing medicines law to take measures to improve the accessibility of medicines (such as the provisions to allow parallel importation), nor has it made the necessary legislative amendments consequent to the flexibilities provided in the Doha Declaration and subsequent August 30 2003 Agreement (World Trade Organization Council for TRIPS, 2003; World Trade Organization, 2001).

Finally, the tension between the attainment of human rights (in particular, the right to access health care) and trade and intellectual property rules which impede the realisation of those rights, will not be resolved if medicines continue to be viewed as private items of consumption. It is increasingly being contended that medicines, already subject to a significant degree of regulation, must be construed as public goods because of their critical public health and public interest impacts (Parmet, 2006).

## **V.2 The Constitutional Framework**

The post-apartheid South African Constitution contains several provisions dealing with socio-economic rights in general, and health

rights in particular (Republic of South Africa, 1996). These include the right to access health care (section 27), bodily and psychological integrity (section 12(2)), privacy (section 14(a)), and to an environment that is not harmful to health or well-being (section 24(a)). In addition, the state must respect, protect, promote and fulfil the rights in the Bill of Rights (section 7(2)), including socio-economic rights. These obligations collectively mean that the state is required to not only refrain from the unfair and unreasonable curtailment of a person's rights, but also to take proactive measures to, for example, develop and implement a comprehensive legal framework for the realisation of those rights, and to create the necessary conditions under which individuals may be capacitated to themselves realise those rights. Most importantly, it provides that everyone has the right to have access to health care services, and that the state must take reasonable legislative and other measures, within its available resources, to achieve the progressive realisation of this right (sections 27(1) and (2)).

The right is, however, subject to two important qualifications, namely, that it must be progressively realised, and that it is subject to available resources. The leading decision on the issue of access to medicines is undoubtedly the TAC case (*Minister of Health & Others v Treatment Action Campaign & Others* 2002 (5) SA 721 (CC) and *Minister of Health and Others v Treatment Action Campaign and Others* (no 2) 2002 (5) SA 717; 2002 (10) BCLR 1033 (CC)). Firstly, the judgment affirmed the centrality of access to medicines in the realisation of the right of access to health care. Secondly, it recognised that constraints on the public purse are not necessarily an impediment to the realisation of rights. Thirdly, the court stood firm on the challenge to its authority to make pronouncements on policy matters, in various guises, notably under the 'separation of powers' doctrine. It recognised that disputes over socio-economic rights invariably required the evaluation of state policy and an order for 'appropriate relief' where such policy is inconsistent with the Constitution, which could include mandatory orders and supervisory jurisdiction or structural interdicts. Finally, the decision elaborated the understanding of the concept of 'progressive realisation of rights' as not merely signifying 'pious wishes' but entailing a serious commitment to the delivery of health care services (Mathipa and Budlender, 2002).

The TAC decision has paved the way for a significant access to medicines jurisprudence, and in its wake, a number of critical questions arise in relation to intellectual property provisions in the law:

- Given the high costs of antiretrovirals (ARVs), would the measures necessary to contain the HIV/AIDS pandemic include the issuing of compulsory licences to facilitate the manufacture and importation of cheaper medicines?
- Is this interference with the rights of pharmaceutical patent holders constitutionally tenable? Or does it violate their protected private property interests (defined in section 25)?

In trying to decide whether issuing compulsory licences is reasonable, the intent of the legislature might be a guide. These measures were included in patent law precisely to make inventions (including medicines) accessible, for example in the event of abuse of patent. South Africa also has competition legislation, the Competition Act which permits divestiture as a remedy for anti-competitive practices. In addition, section 15C of the Medicines and Related Substances Act allows the minister to enable parallel importation in order to facilitate affordable access to medicines and other products. The test of reasonableness entails a balancing of interests, the public interest of saving lives taking precedence over the private commercial interests of the patent holder. Should there be a conflict between the right to health and private property protection, “constitutional right will always trump policy” (Davis, 1992). This principle has also been tested in law (*Ex parte* Chairperson of the Constitutional Assembly: *In re* Certification of the Constitution of the Republic of South Africa 1996 (4) SA 744 (CC)).

### **V.3 Components of South Africa’s Patent Regime**

Compliance with the TRIPS Agreement required relatively few, though critical amendments in 1997. The key relevant features of the patent regime are recounted below.

#### Patent standards

The Patents Act provides that a patent “may be granted for any new invention which involves an inventive step and which is capable of being used or applied in trade or industry or agriculture” (section 25(1)).



### Novelty

Novelty requires that the invention be new, namely, that it has not been previously described (usually in writing) or widely used. As regards this requirement, the Act states that “an invention shall be deemed to be new if it does not form part of the state of the art immediately before the priority date of that invention” (section 25(5)).

### Inventiveness

An invention is deemed to involve an inventive step “if it is not obvious to a person skilled in the art” having regard to any matter already available to the public (section 25(10)). In other words, it must be a step beyond routine discovery, or more than the mere adding together of previously known products or processes (for example, *Gentiruco AG v Firestone SA (Pty) Ltd* 1971 BP 58 (A) 172). In accordance with a court decision, “the objection based on a lack of inventiveness is one of long standing in our patent law” (*Ensign-Bickford (South Africa)(Pty) Limited and Others v AECI Explosives and Chemicals Limited* 1998 BIP271 (SCA) 281).

### New uses of an invention

Having considered the parameters of what is patentable, the question which arises is: in defining patentability criteria in respect of medicines, should new uses of the invention (other than its originally intended use) or new forms (for example, use in paediatric as opposed to adult therapy) be excluded from patentability? Would such instances constitute novelty and an inventive step? In general, the position South African courts have adopted is that once a substance forms part of the state of the art, a new or second use thereof will not make it eligible for a new patent (Burrell, 1999). This interpretation is consistent with the relative freedom countries are accorded to opt for higher standards for the requirement of inventiveness (UNCTAD and ICTSD, 2005). India is a good example of how this flexibility has been utilized, where section 3(d) disallows the patenting of a new form of a known substance which does not result in enhanced efficacy, or a new use of a known substance or process (Republic of India, 2005). However, as South Africa does not have an examination system for patent applications, the appropriate standard is not likely to be observed, unless subjected to a legal challenge through revocation or infringement proceedings (such as in *H Lundbeck A/S & Another v Cipla Medpro (Pty) Ltd* 2008 BIP 79).

### Industrial applicability

The requirement that the invention must be one “which is capable of being used or applied in trade or industry or agriculture” (section 25(1)) resonates with that of utility found in many jurisdictions. South African courts have held that ‘useful’ bears the ‘special meaning of effective to produce the result aimed at’ or promised (Burrell, 1999). In other words, to be ‘useful’ any suitably knowledgeable person following the specifications of the patent must be able to make the invention.

### Disclosure

The South African equivalent of the disclosure provision spells out the contents of a specification in some detail, requiring an abstract; a sufficient description illustrating or exemplifying the invention and the manner of performance; and the claim(s) defining the invention, which have to be clear and fairly based on the matter disclosed in the specification (sections 32(3) and 32(4)).

### Opposition procedures

South African legislation makes no provision for opposition procedures, limiting the examination of applications and specifications to the Registrar of Patents, who is empowered to grant the application if it complies with the requirements of the Act (section 34). However, inspection by the public is permitted after the patent has been sealed and granted.

Furthermore, there appears to be a complete lack of transparency in the patent examination process, as the statute merely requires the registrar to conduct a formal tick-box approach to an application (section 34). Given that patent grants, particularly in the case of essential medicines, have such far-reaching impacts on the broader public, the process ought to accommodate public scrutiny and comment. Perhaps the best method of achieving this participation is through the opportunity to file a pre-grant opposition. Once again, the Indian experience is instructive, where sections 25(1) and 25(2) of the Indian Patent Act provide for both pre- and post-grant opposition (Republic of India, 2005).

### Exclusions from patentability

South African legislation covers most of the exclusions outlined by TRIPS Article 27, namely, inventions which encourage offensive or immoral behaviour (section 25(4)(a), any plant or animal variety or any essentially biological process for their production excluding a microbiological process or its product (section 25(4)(9b)), as well as any surgical, therapeutic or diagnostic method of treatment of humans or animals (section 25(11)). Furthermore, the Patents Act empowers the Registrar of Patents to refuse any application that is frivolous; or whose use encourages illegal, immoral and offensive behaviour, including publication or exploitation (section 36). As the concepts of morality and offensive behaviour are relative concepts, particularly in a diverse and evolving society such as South Africa, it is unclear how this provision is to be applied.

### Exceptions

There is no general provision in South African law of the order of Article 30 of TRIPS, but through its provisions relating to infringement, the Patents Act specifies two instances of exceptions: the use of patented inventions aboard convention vessels, aircraft or land vehicles temporarily or accidentally within territorial waters or in the Republic, and the making, use, exercise, disposal, offer to dispose and importing of the patented invention for purposes of obtaining regulatory approval for the manufacture, production, distribution, use or sale of any product (sections 69 and 69A of the Patents Act). The latter, Bolar-type exception, allows a generic producer, seeking to register a follow-on equivalent of a previously approved or registered medicine, to begin product development and compilation of the required registration dossier even before a patent has expired.

South African legislation is, however, lacking to the extent that it makes no provision for educational, experimental and research exceptions, nor for the export of an invention manufactured on a non-commercial scale in pursuance of the early working exception.

### Compulsory licensing

The Patents Act permits the granting of compulsory licences under two broad categories: for dependent patents (section 55) and in instances of abuse of patent rights (section 56). The latter is of more direct

significance to access to medicines. It sets out four circumstances under which patent rights are deemed to be abused, namely:

- If the patented invention is not being worked in the Republic on a commercial scale or to an adequate extent.
- If the demand for the patented article in the Republic is not being met to an adequate extent and on reasonable terms.
- If the refusal of the patentee to grant a licence on reasonable terms prejudices trade, industry or agriculture.
- If the demand in the Republic for the patented article is being met by importation and the price is excessive compared to the price in the country of manufacture.

No compulsory licences have been granted to date on pharmaceutical products in South Africa although there are many reported decisions on the issue. For example, the Supreme Court of Appeal rejected an application for a compulsory licence on the grounds of abuse of patent, being non-working and failure to license (*Syntheta (Pty) Ltd v Janssen Pharmaceutica NV & Another* 1999 (1) SA 85 SCA) on the grounds that the applicant had not placed sufficient information before it to establish the alleged abuse.

Finally, on the issue of compulsory licences, South African law has not incorporated the important flexibility contained in the Doha Declaration facilitating such licences for public health emergencies.

### Government use

Section 4 of the Patents Act provides that “a Minister of State may use an invention for public purposes on such conditions as may be agreed upon with the patentee, or in default of agreement on such conditions as are determined by the commissioner on application by or on behalf of such Minister and after hearing the patentee”. Further, section 78 states that “The Minister may, on behalf of the State, acquire, on such terms and conditions as may be agreed upon, any invention or patent”. Under section 25(2) of the Constitution, the government could also ‘take’ or expropriate the patent subject to just compensation.

### Voluntary licences

In South African law, a voluntary licence is an “authorisation given by a patentee to another to invade the patent monopoly with impunity”

(Burrell, 1999). A voluntary licence may take one of three forms: non-exclusive (where the patentee may still grant licences to others); exclusive (all others, including the patentee, are excluded); and sole (all others, with the exception of the patentee, are excluded) (Burrell, 1999). The best-known cases of voluntary licences in respect of pharmaceuticals are those granted as part of the settlement of the Competition Commission complaint against GlaxoSmithKline and Boehringer Ingelheim, in favour of local companies (*Hazel Tau & Others v GlaxoSmithKline & Boehringer Ingelheim* (Case no. 2002Sep226)). Although subsequent applications by generic manufacturers for voluntary licences on other antiretrovirals were successful, this was not always the case (Avafia et al., 2006).

### Parallel importation

South African law recognises the doctrine of exhaustion, although the Patents Act did not make explicit provision for it until recently. It had been left to the judiciary, drawing on the jurisprudence of the UK and the USA, to enunciate the rules governing exhaustion (*Stauffer Chemical Co v Agricura Ltd* 1979 BP 168 (CP)). The 2002 amendments to the Patents Act saw the introduction of a provision permitting parallel importation (Republic of South Africa, 2002).

Furthermore, the 1997 amendments to the Medicines Act expressly introduced a provision authorising the Minister of Health to remove patent protection on medicines put on the market by the owner or with his consent, effectively permitting parallel importation (Republic of South Africa, 1997b). As to whether this included the importation of generic medicines legitimately produced under a compulsory licence became the subject of the litigation by the pharmaceutical industry against the government. This issue was settled by the promulgation of regulations which specify the conditions under which parallel importation may take place. Another grey area is whether the TRIPS Agreement requires parallel importation to be limited to patented products, and indeed, Kenya's 'liberal' provisions in this respect appear to have passed muster with the TRIPS Council review for compliance (Lewis-Lettington and Banda, 2004).

### Revocation of patent

The issue of revocation has particular currency in the South African context, given that patent applications are not subjected to examination and scrutiny as to their merits. The Patents Act makes provision for patents to be revoked on the grounds of ineligibility of the patentee, patent granted in fraud of another's rights, non-patentability of the invention, inability of performance of the invention as illustrated in the specification, incompleteness of the method of performance, claims in the specification not being clear or not fairly based on matter disclosed, intentionally false representation in the application, frivolity or offensive or immoral use of the invention or claims of a microbiological process or product as an invention (section 61(1) and where a patentee makes a false declaration as to the origin of indigenous biological resources and his or her authority to use same (Republic of South Africa, 2005).

The grounds available are notably ones that relate to a fraudulent act, mistake, or non-disclosure of complete specifications. What is conspicuously lacking is the possibility of revocation in the case of abuse of patent, as provided for in Article 5A of the Paris Convention on Intellectual Property of 1883.

## **V.4 Competition Law**

The exercise of intellectual property rights, to the extent that they create monopolies, may give rise to anti-competitive behaviour either by individual companies, or through collusive activity. Competition law and policy as a strategy to access medicines is a relatively new development in South Africa. In at least one Competition Commission ruling, innovator companies have been found to have engaged in anti-competitive conduct, and thereby abused their patents, by charging excessive prices and denying a competitor access to an essential facility (Hazel Tau case). Competition law thus provides another effective sanction against patent abuse in the form of an anti-competitive compulsory licence, which is consistent with Article 31(k) of TRIPS and is, further, not subject to the domestic use and prior negotiations requirements.

## **V.5 Data Protection**

Protection of clinical trial data in South Africa predates its inclusion in the TRIPS Agreement, which requires that undisclosed clinical trial data must be protected against unfair commercial use and disclosure (Article 39). In line with the practice of regulatory authorities worldwide, the Medicines Control Council (MCC) does not publicly disclose or share data submitted for registration purposes. However, when considering an application for the registration of a generic equivalent, the MCC does not require the applicant to furnish any new data on the safety and efficacy of the drug, but merely on the quality of the generic (Gray, 2007). Data presented before is not directly accessed or cross-referenced, but exemption from providing such data is allowed. There is no obligation on members to grant exclusive rights over data, as is the case in the US, the EU and other countries (Correa, 2006). The effect of such protection is that generic producers are “precluded from relying on pre-existing data to establish safety and efficacy even when the producer has evidence that the two drugs are bioequivalent.” (Druce et al., 2004)

The issue of data protection has gained greater prominence because of its inclusion in Free Trade Agreements. Many FTAs require the parties to grant data exclusivity rights for a minimum of 5 years irrespective of whether a patent is issued or not, or whether the invention is undisclosed or not. Following the collapse of the FTA negotiations between the US and the Southern African Customs Union (SACU) the pressure to adopt stringent data exclusivity rules has eased (Vawda, 2007).

In keeping with the imperative to incorporate all available flexibilities in the international intellectual property and regulatory regimes to advance the agenda of universal access to medicines, South Africa should legislate to secure the right of MCC to rely on the innovator’s data when considering applications for generic medicines without direct cross-reference to such data. Public health interests demand that data protection be limited strictly to the parameters outlined in Article 39.3 of TRIPS.

## **V.6 Concluding Comment on the Intellectual Property Regime**

The changes introduced in South Africa's law as a result of TRIPS thus included, in the main, the extension of patent protection for a period of 20 years (previously 16 years); and the removal, as a ground for compulsory licensing, of the situation where the commercial working of an invention was being hindered by importation of the patented article. Also introduced were provisions for the use of the regulatory early working exception, the deletion of the requirement of disclosure of the best method of performing the invention known to the applicant at the time the application is lodged, and the further lowering of the disclosure standard by amending the requirement for the specification to be 'fully' described to 'sufficiently' described. Significantly, a provision has been introduced to effectively permit parallel importation.

Nonetheless, important flexibilities have not been incorporated in the legislation, notably those relating to compulsory licences for public health purposes, strictures on patenting standards, provisions for the use of the Paragraph 6 Decision; educational, research and experimental exceptions to patent rights, increasing the grounds for revocation of patents; and provision for opposition procedures to patent applications both before and after grant. In all these respects, the legal framework for intellectual property protection in South Africa can still be improved to considerably enhance access to medicines. While free trade negotiations in which South Africa was a participant have stalled, this potential threat to a pro-access intellectual property system still exists. South Africa can expect to come under increasing pressure to provide linkages between patent status and medicines' regulatory approval and also to increase data protection measures.

## **VI. ANALYSIS OF THE PHARMACEUTICAL PATENT DATABASE**

The South African Patent Journals for 2008 were searched, and some 2442 pharmaceutical patents identified and entered into the database. This data is now analysed according to key variables.

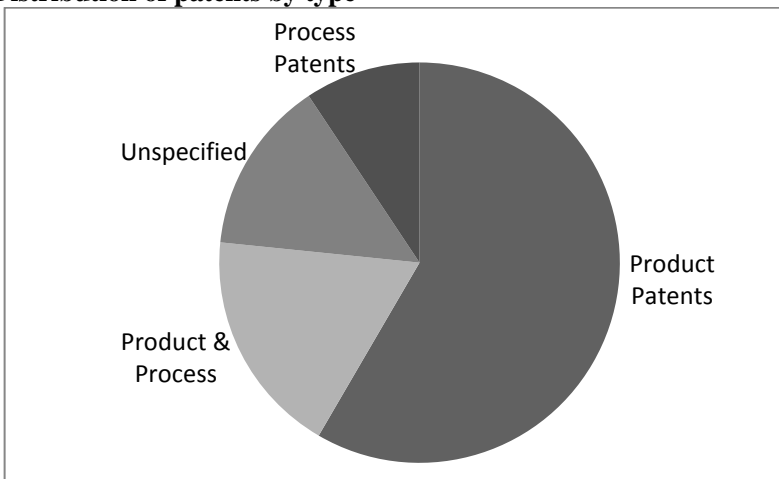


Distribution of pharmaceutical patents by type (2008)

Of the pharmaceutical patents identified in the year 2008, 1426 (58 per cent) were for products, 445 (18 per cent) for product and process, 228 (10 per cent) for process, and 343 (14 per cent) were unspecified.

Figure 10

**Distribution of patents by type**



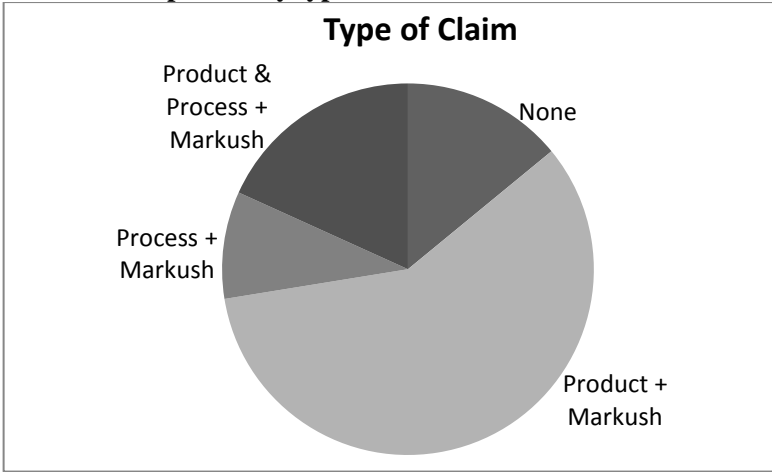
Distribution of pharmaceutical patents by therapeutic class

Of the selected group, 445 (18 per cent) were for antineoplastic and immunomodulating agents, 325 (13 per cent) for nervous system, 308 (13 per cent) for anti-infectives for systemic use, 173 (7 per cent) for alimentary tract and metabolism, 151 (6 per cent) for cardiovascular system, 111 (5 per cent) for musculo-skeletal system, 81 (3 per cent) for genito-urinary system and sex hormones, 76 (3 per cent) for respiratory system, 63 (3 per cent) for blood and blood-forming organs, 46 (2 per cent) for dermatologicals, 33 (1 per cent) for sensory organs, 19 (0.7 per cent) for various classes, 18 (0.7 per cent) for systemic hormonal preparations, excluding sex hormones and insulins, 6 (0.1 per cent) for anti-parasitic products, insecticides and repellents, and 587 (24.5 per cent) were unspecified.

Distribution of patents by type of claim, including Markush Claims

Figure 11

**Distribution of patents by type and Markush Claims**



Distribution of patents by therapeutic use

Table 1

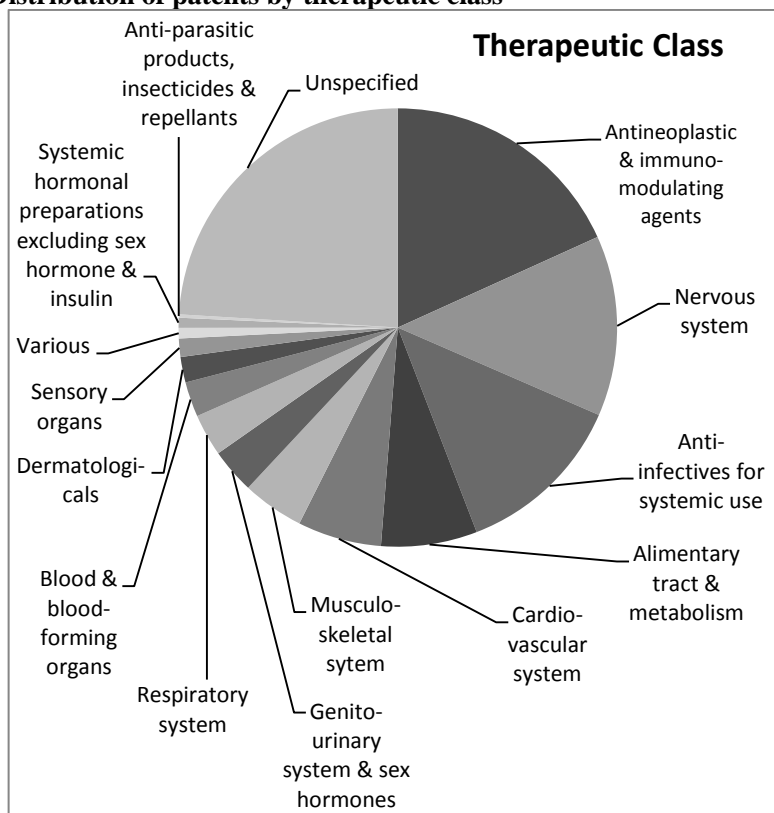
**Distribution of patents by therapeutic use**

<b>Therapeutic use</b>	<b>Number of patents</b>
Anti-neoplastic & immunomodulating agents	445
Nervous system	325
Anti-infectives for systemic use	308
Alimentary tract & metabolism	173
Cardiovascular system	151
Musculo-skeletal system	111
Genito-urinary system & sex hormones	81
Respiratory system	76
Blood & blood-forming organs	63
Dermatologicals	46
Sensory organs	33

Therapeutic use	Number of patents
Various	19
Systemic hormonal preparations excluding sex hormone & insulin	18
Anti-parasitic products, insecticides & repellents	6
Unspecified	587

Figure 12

**Distribution of patents by therapeutic class**



Patents held by companies by country of origin

The USA was the leading country of origin for the patents with 1208, followed by the UK 234, Germany 166, France 107, Japan 83, Switzerland 82, Sweden 80, India 59, Denmark 51, Netherlands 34, Italy 26, South Africa 16, China 12, and Brazil 1. The country of origin was not identifiable in 137 cases.

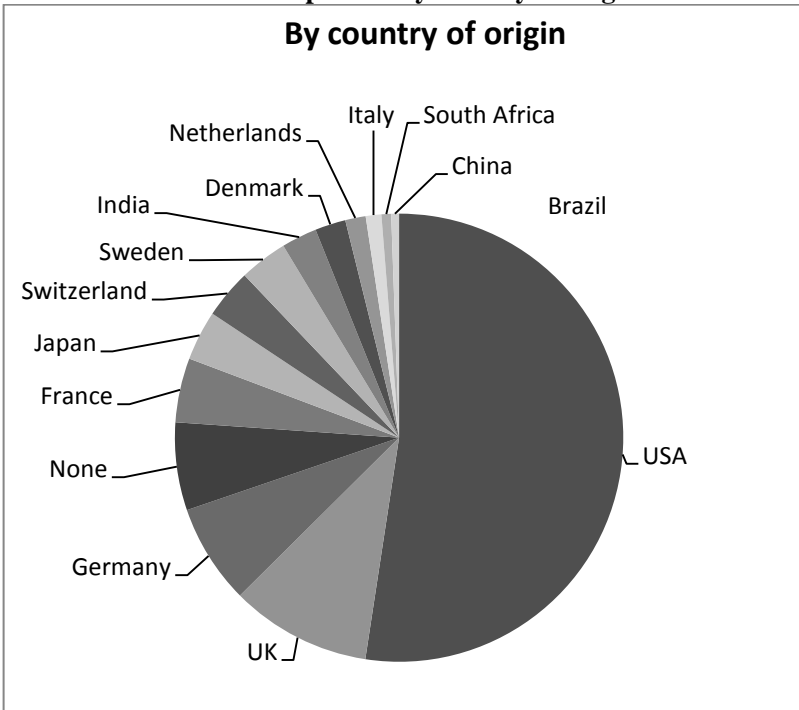
Table 2

**Holders of South African patents by country**

Country	Origin	Number	Percentage
South Africa	United States	1208	49
South Africa	United Kingdom	234	10
South Africa	Germany	166	7
South Africa	None	146	6
South Africa	France	107	4
South Africa	Japan	83	3
South Africa	Switzerland	82	3
South Africa	Sweden	80	3
South Africa	India	59	2
South Africa	Denmark	51	2
South Africa	Netherlands	34	1
South Africa	Italy	26	1
South Africa	South Africa	16	1
South Africa	China	12	0.5
South Africa	Brazil	1	0.05

Figure 13

**Holders of South African patents by country of origin**



Distribution by type of patent for leading countries

The USA is the leading country of origin for the majority of patent holders.

Of the 1208 patents held by US companies, 729 (60 per cent) were for products, 93 (8 per cent) for process, 185 (15 per cent) for product and process, and 201 (17 per cent) were unspecified.

A similar pattern emerges in respect of patents held by United Kingdom holders of patents registered in South Africa.

Figure 14  
**Patents held by US holders, by type**

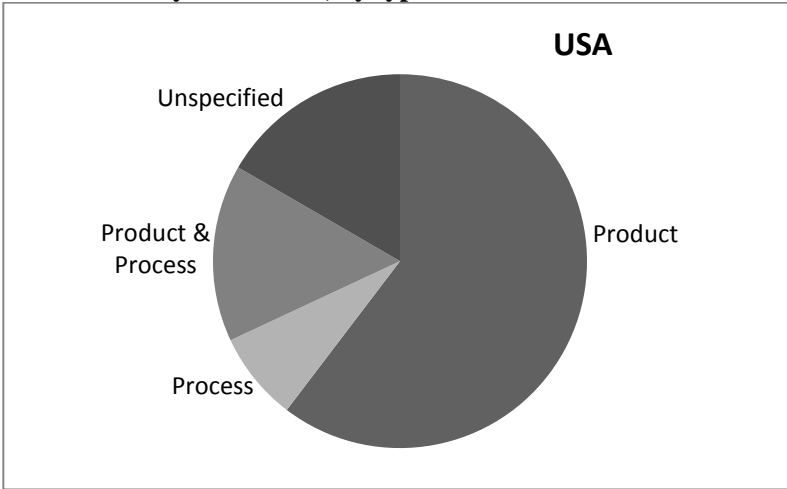
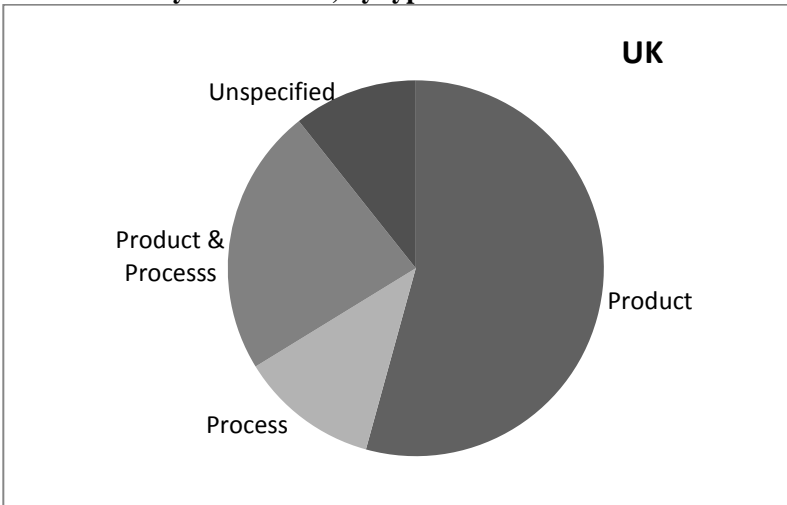


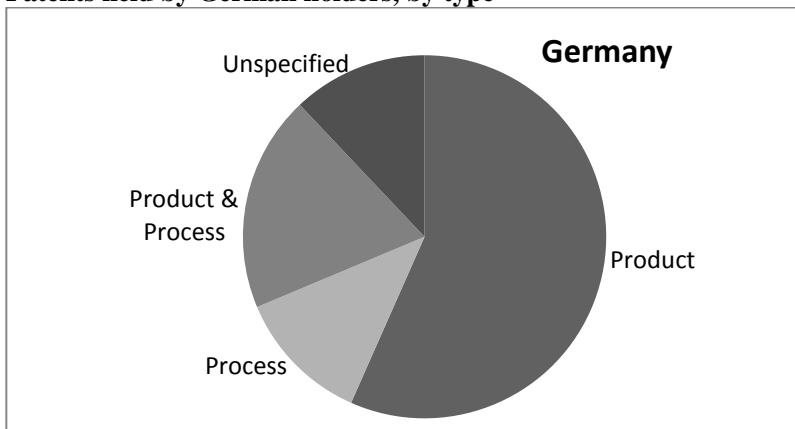
Figure 15  
**Patents held by UK holders, by type**



Of the 234 patents held by UK companies, 127 (54 per cent) were for products, 28 (12 per cent) for process, 54 (23 per cent) for product and process, and 25 (11 per cent) were unspecified.

Figure 16

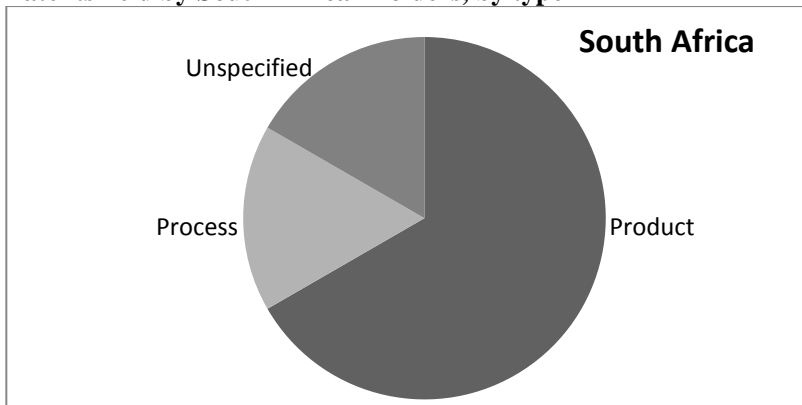
**Patents held by German holders, by type**



Of the 166 patents held by German companies, 94 (57 per cent) were for products, 20 (12 per cent) for process, 32 were for product and process, and 20 (12 per cent) were unspecified.

Figure 17

**Patents held by South African holders, by type**



Of the patents held by South African companies, 8 (67 per cent) were for products, 2 (17 per cent) for process, and 2 (17 per cent) were unspecified.

Table 3

**Schedule of patents held by South African holders**

Patent number	Expiry date	Title	Applicant	Therapeutic class	Type	INN
2005/07739	25.09.25	Novel composition relating to treatment of allergies	Pharmachoice Healthcare (Pty) Limited.	R	Product	
2006/01622	11.12.27	Treatment preparation and method for cell-based myocardial regenerative therapy	Bio Hrxt (Pty) Ltd.	C	Product	
2006/03135	19.04.26	Skin burn treatment ointment	Irene Elizabeth Snyman	D	Product	
2007/01036	17.07.25	Anti-histaminic composition	APL Cartons (Proprietary) Limited	R	Product	
2007/04160	21.05.27	Treatment of parasitic infections in humans and animals	South African Medical Research Council, University of Cape Town	P	Process	
2006/09113	31.10.26	A method for detecting mycobacterial infection	University of Pretoria	J	–	
2007/01932	05.03.27	Pharmaceutical composition	Bayer Healthcare AG	–	Product	
2006/07508	07.09.26	Pharmaceutical composition	Gast, Kevin	–	Process	
2007/10786	12.12.27	Heterogeneous-ly configured	University of the	–	Product	



		multiparticulate gastrointestinal drug delivery system	Witwatersrand, Johannesburg			
2007/06393	31.01.26	Method for determining HIV-1 viral load	National Health Laboratory Service, University of the Witwatersrand, Johannesburg	J	–	
2007/01933	05.03.27	Pharmaceutical composition in the form of a water soluble solid dosage form	Bayer Healthcare AG	–	Product	
2007/05708	10.07.27	A composition	Vermeur Willem Adriaan	L	Product	

#### Distribution of patents by companies

The leading patent holders are listed below.

Table 4

#### **Schedule of leading holders of South African patents (2008)**

<b>Company</b>	<b>Country</b>	<b>Number of patents</b>	<b>Percentage of total grant</b>
AstraZeneca	UK	88	4
Novartis AG	Switzerland	49	2
Wyeth	US	43	2
F Hoffmann-La Roche AG	Switzerland	35	1
Pfizer Products Inc.	US	32	1
Merck Patent GmbH	Germany	29	1
Various	South Africa	12	0.5

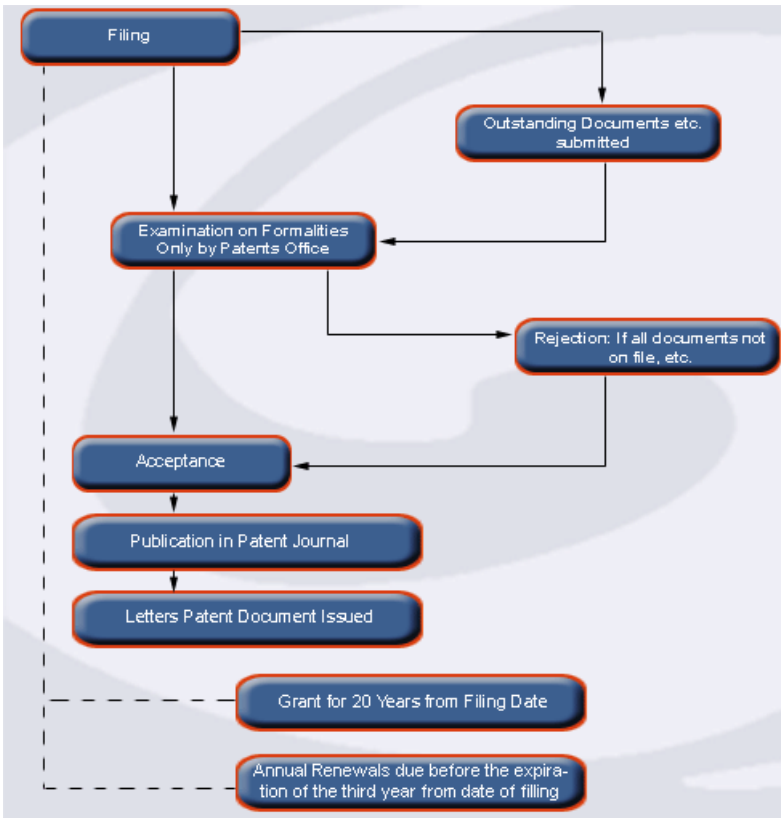
## VII. 'TRANSPARENCY' OF THE PATENT SYSTEM

### Patent Registration procedure

The following figure illustrates the procedure followed in the grant of a patent.

Figure 18

### **Procedure for patent grant**



Source: CIPRO

[http://www.cipro.gov.za/products\\_services/patents\\_registration.asp](http://www.cipro.gov.za/products_services/patents_registration.asp).

The South African equivalent of the patent office is the Companies and Intellectual Property Registration Office (CIPRO), a division within the Department of Trade and Industries. The Office specifies a three-step procedure for the registration of a patent, with a formal examination procedure usually taking up to six months from the filing of a complete application. Once the formalities have been complied with, the application is accepted and the applicant is required to publish the patent in the *Patents Journal* which, according to the CIPRO website ‘allows members of the public to lodge objections’ within three months. If there are no objections, the Patents Registrar will issue a Patent Certificate (Department of Trade and Industry). This information appears to be misleading as the Act makes no provision for opposition, and a patent is automatically sealed on acceptance by the Registrar (Burrell, 1999). In effect, CIPRO is a non-examining office, with applications being approved provided they comply with the formal requirements (Zdrakova, 2009). This is a major drawback as it has the potential to admit patents of low or inferior quality, meaning that they may not entirely satisfy the requirements of novelty, inventive step and industrial applicability rigorously interpreted and applied.

## **VIII. PATENT LITIGATION**

A review of court proceedings revealed that only a small number of pharmaceutical patent challenges have been reported in the case law. These statistics are limited to matters which are brought to court, and do not include cases which might have been settled out of court.

Table 5 gives a summary of South African patent litigations for the period from 2003-2008.

Table 5

**Schedule of South African patent litigation for the period 2003-2008**

<b>Case number</b>	<b>Parties</b>	<b>Patent number</b>	<b>Patents/ products involved</b>	<b>Outcome</b>	<b>Rationale</b>
2003 BIP 5	Glaxo Group Ltd v Cipla-Medpro (Pty) Ltd	92/9167	Aerosol formulation for use in medicaments by inhalation	Application granted to suspend an application for revocation of patent until pending application for amendment of patent decided.	Important for status of patent to be determined first, thus amendment, but respondent still able to apply for revocation.
2005 BIP 1	Pfizer Ltd & Another v Cipla Medpro (Pty) Ltd & Others	87/2439	NORVASCO (active ingredient besylate salt of amlodipine)	Application granted in order to (a) Correct certain clerical errors in the patent claims, and (b) Interdict respondents being generic producers of NORTWIN (having same active ingredient),	The court accepted that the errors were inadvertent clerical errors. Regarding the interdict the court felt the applicant's prospects in the revocation were favourable, and any prejudice to respondent was of its

<b>Case number</b>	<b>Parties</b>	<b>Patent number</b>	<b>Patents/ products involved</b>	<b>Outcome</b>	<b>Rationale</b>
				from marketing the same, pending revocation proceedings.	own making.
2007 BIP 59	Glaxo Group Ltd v Cipla Medpro (Pty) Ltd & Others	90/7136	Medicaments relating to treatment of asthma & other respiratory disorders	Application granted to strike out irregular opposition procedure to the patent holder's application for amendment of patent, while revocation proceedings pending.	Advertisement by applicant superficially confusing, but could readily be clarified; respondent used irregular procedure.
2007 BIP 66	Glaxo Group Ltd v Cipla Medpro (Pty) Ltd & Others	90/7136	Medicaments relating to treatment of asthma & other respiratory disorders	Respondent granted leave to intervene in an application to amend the patent.	Leave to intervene granted as respondent showed clear intention to oppose application to amend.

<b>Case number</b>	<b>Parties</b>	<b>Patent number</b>	<b>Patents/ products involved</b>	<b>Outcome</b>	<b>Rationale</b>
2007 BIP 91	Glaxo Group Ltd v Cipla Medpro (Pty) Ltd & Others	90/7136	Medicaments relating to treatment of asthma & other respiratory disorders	Application to amend the patent while revocation proceedings pending granted; and respondent's application for postponement of the amendment application refused.	No culpable conduct on part of applicant to warrant the exercise of court's discretion to order postponement.
2008 BIP 79	H Lundbeck A/S & Another v Cipla Medpro (Pty) Ltd	89/4476	Escitalopram (marketed as Cipralext)	Application refused for (a) Correction of clerical errors in, or amendment of, claims of patent, and (b) Interdict to restrain generic producer of escitalopram from marketing same.	Made distinction between clerical errors (can be corrected) and invalid claim (insurmountable obstacle) and applicants failed to establish distinction. Applicant aware of errors for long time but only sought to

<b>Case number</b>	<b>Parties</b>	<b>Patent number</b>	<b>Patents/ products involved</b>	<b>Outcome</b>	<b>Rationale</b>
					remedy when respondent launched competing product. Amendment sought to introduce claim not fairly based on matter disclosed in specification.
2008 BIP 107	H Lundbeck A/S & Another v Cipla Medpro (Pty) Ltd	89/4476	Escitalopram (marketed as Cipralext)	Application refused for (a) Amendment of patent, and (b) Temporary interdict restraining respondent from selling generic product Lexamil.	Refused, because absent grant of amendment, patent could not be enforced. As remaining term only 8 months, application was in fact for a final interdict.

The following observations may be made from the foregoing data:

- In contrast to the large number of pharmaceutical patents granted (more than 2400 for 2008 alone), the volume of litigation is minute.
- The fact that there is no patent examination system results in an inordinately large number of ‘weak’ patents, as well as closes the opportunity for pre- and post-grant opposition proceedings.
- Thus patents are litigated primarily through applications to revoke, or where the holder alleges infringement.
- In the instances where revocation proceedings have been initiated on the basis that the patent is unclear and not obvious (*Pfizer & Ano v Cipla Medpro & Ors* 2005 BIP 1), the court refused to revoke, accepting that the besylate salt was itself unexpected, constituted an advance on the prior art, and represented an inventive step forward.
- Thus, despite the provisions of the Patents Act which set a high standard for patentability, the courts are applying a fairly low standard for patentability.

## **IX. CONCLUSION**

Health and medicines regime:

- Some 82 per cent of the population is dependent on the public health system for access to health care.
- However, of the almost 9 per cent of GDP spent in 2009 on health, 5.2 per cent was in the private sector (serving about 18 per cent of the population) and 3.7 per cent in the public sector (serving 82 per cent).

Pharmaceutical market and production:

- South Africa has a highly developed pharmaceutical system, with considerable local capacity, some generic manufacturers having been in existence for over 100 years.



- But local research and development is largely restricted to formulation issues, with some new drug discovery projects in public-private partnerships and academic research centres.
- South African companies control 39 per cent of the local market, with foreign companies predominating with 61 per cent.
- The leading individual company is South African – Aspen Pharmacare – with 17 per cent of market share.

Medicines regulation:

- The medicines regulator is the Medicines Control Council which assesses medicines for registration following the criteria of quality, efficacy and safety.
- The public health sector uses predominantly generic products, with some occasional branded medicines.
- There is a limited degree of price regulation, exercised on the private sector by the Minister of Health.
- Since 2003, the requirement of the mandatory offer of generic substitution, in order to promote the use of cheaper generics, has been applied.
- Generics account for about 50 per cent of the private sector share, by volume.

Intellectual property protection:

- The essential requirements for the grant of a patent are: novelty, inventive step and industrial applicability.
- New uses and new forms are not patentable, once the substance forms part of the state of the art.
- However, since South Africa has a non-examining system, this (theoretical) high standard is not maintained.
- No opposition procedures are available.
- Some exceptions (early working) are available, but there is no research exception.
- There are substantial provisions for compulsory licences and government use orders, although these provisions have not been used in respect of a single pharmaceutical product.

- Parallel importation is permitted, the country subscribing to the international exhaustion regime.
- There is a progressive competition law framework, and strong action has been taken against abusive and collusive practices by several, including pharmaceutical, companies. This area of law has proven to be the most effective legal remedy thus far for increasing access to medicines.
- Data for clinical trials enjoy protection from public disclosure, but are referenced for the approval of generic follow-ons.

Analysis of database:

- 58 per cent of the patents were for products; 18 per cent for products and processes; 10 per cent for processes; and 14 per cent were unspecified.
- The main therapeutic class comprising the patents were: anti-neoplastic and immunomodulating agents (18 per cent); nervous system (13 per cent); anti-infectives for systemic use (13 per cent); alimentary tract and metabolism (7 per cent); cardio-vascular system (6 per cent); musculo-skeletal system (5 per cent); genito-urinary system and sex hormones (3 per cent); respiratory system (3 per cent); blood and blood-forming organs (3 per cent); dermatologicals (2 per cent); sensory organs (1 per cent); systemic hormonal preparations, excluding sex hormones and insulin, and anti-parasitics (1.5 per cent); and unspecified by type were (24.5 per cent).
- In terms of country of origin, the USA leads (with 49 per cent), followed by the UK (10 per cent); Germany (7 per cent); No country indicated (6 per cent); France (4 per cent); Japan (3 per cent); Switzerland (3 per cent); Sweden (3 per cent); India (2 per cent); Denmark (2 per cent); Netherlands (1 per cent); Italy (1 per cent); South Africa (1 per cent); China (0.5 per cent); and Brazil (0.1 per cent).

Transparency:








- South Africa does not have an examination system, but rather follows a formality-based approach.












- It takes between 6 months and 1 year to approve a patent.

Litigation:












- While a large number of patents are granted each year, the level of litigation is minute.
- This results in the granting of a large number of ‘weak’ patents, as the courts have been applying a fairly low patentability standards, especially when it comes to new forms of existing compounds.









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# CHAPTER 7

## PROMOTING LOCAL PHARMACEUTICAL CAPACITY IN DEVELOPING COUNTRIES: A DISCUSSION ON INVENTIVE STEP AND COMPULSORY LICENSING

Padmashree Gehl Sampath

### I. INTRODUCTION

Patents over minor variations of existing products have been proliferating in recent times, prompting a discourse not only on the impact of applying lax patenting criteria from a global welfare perspective, but also on what this might mean for knowledge acquisition and technological change in developing countries in particular.

<sup>1</sup> Whereas Article 27 of the Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS) specifies that ‘novelty’, ‘industrial applicability/utility’ and ‘inventive step’<sup>2</sup> are the criteria for grant of patents, the provision does not define these criteria. As a result, they can be interpreted in different ways within national regimes. At a fundamental level, the freedom to decide what constitutes novelty and what the level of inventive step should be in order that an invention can be granted a patent represents a flexibility in the TRIPS Agreement that can be utilized to address the broader interests of society (Reichman, 1997; Correa, 2000; CIPR, (2002).

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<sup>1</sup> Protection has been extended from inventive activity to mere discoveries and from pure inventive activity (that embodied information on a particular technology) to information on just scientific information (see Forero-Pineda, 2006; David, 2000). Reichman (2000) tracing this trend, notes that this is related to the changed nature of innovation itself in the post-computer industry context, where such small-grained inventions are granted patent rights in order to secure lead advantages to those who get it right first from increased competition.

<sup>2</sup> Also known in the USA as non-obviousness with some differences in definition and application.



The trend towards patents on minor variations of products has been made possible by developments in patent laws in several developed countries, especially in the USA and to a lesser extent in the EU, that lower the requirement of inventive step. Accompanied by the expansion of patenting to newer areas, such as business and financial innovations in the USA,<sup>3</sup> these trends are stretching the boundaries of what can be patented and whether or not this is indeed in the broader interest of technology within these societies remains to be seen.<sup>4</sup> But it is increasingly becoming clear that these trends carry profound implications for economic catch-up of developing countries by systematically promoting the patenting of incremental innovations that simply extend patent life on products and processes.

Specifically in the pharmaceutical sector, although the number of newly-developed chemical entities has dramatically fallen during the last ten years, the number of patents over simple changes in chemistry/formulation of existing pharmaceutical products (e.g. polymorphs, combinations, dosage forms, isomers) has continuously increased. The global pharmaceutical landscape is becoming increasingly concentrated, and trends indicate the continuation of industry consolidation.<sup>5</sup> In such a context, such patents can be used to exclude generic competition, may block access to affordable drugs and constitute an important obstacle for the realization of the right to health. Patenting of incremental innovations also promotes evergreening<sup>6</sup> and unnecessarily extends the life of the drug in question, affecting the production options of generic companies in developing countries and

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<sup>3</sup> See the *Bilski* case, *In re Bilski*, 545 F.3d 943, 88 U.S.P.Q.2d 1385 (Fed. Cir. 2008). Also see Lerner, 2000 and 2006.

<sup>4</sup> See Reichman and Hasenzahl (2003); CIPR (2002); Jaffe and Lerner (2004 for just a discussion on the USA) and Gallini (2002), among others that explore the issue of whether the recent surge in patenting is beneficial for technological progress and economic growth.

<sup>5</sup> Smith et al (2009, p. 685) note that the ten largest multinational companies account for almost 50 per cent of all pharmaceutical sales globally, and the top 20 MNCs (based in the USA, UK, Germany, France and Switzerland) each have an average of over 100 affiliates in more than 40 countries worldwide (including 19 developing countries).

<sup>6</sup> The term 'evergreening' refers to any means of extending the life of a patent beyond its original term (Smith et al 2009). See Loeffgren (2007) for a discussion on the various means of evergreening.

their profitability. Academics and policy advocates have proposed the adoption of more rigorous criteria to assess patentability in order to avoid the grant of patents that do not make a substantive technical contribution to the state of the art. A few governments have also implemented legislation or policies to this effect.

This paper seeks to move the discussion forward by analyzing some key issues that confront policy makers and academics in this area. First, are there any potential benefits of apply a lax inventive step in the pharmaceutical sector for the local industry, and if so, would such benefits offset the costs associated with the proliferation of patents over minor technical changes? Second, the grant of patents on minor variants of already existing drugs may unnecessarily extend patent monopolies on drugs of importance to public health. The same drugs may then be the subject of compulsory licenses/government use by developing countries, in order to promote the right to access medicinal products of relevance to public health. Can the grant of compulsory licenses for importation be minimized *ex-ante* by simply defining a higher level of inventive step in the pharmaceutical sector? Further, since drugs subject to compulsory licenses/ government use are imported, does a rigorous inventive step also imply greater potential for local firms to engage in generic production and greater health security in the long run?<sup>7</sup> In this context, while there is an extensive body of literature on compulsory licenses/government use as one of the ‘flexibilities’ permitted by the TRIPS Agreement,<sup>8</sup> there is little analysis on the effects of patenting standards (especially the level of inventive step) on the need to use compulsory licensing to address public health issues. If governments were to use and apply more rigorous standards of inventive step in national patent regimes, could the need to expend political capital to issue compulsory licenses for drugs of importance to public health be done away with?

For purposes of the analysis, incremental innovation is understood to mean any minor changes in products and processes that

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<sup>7</sup> Health security is defined here to mean the ability of a country to produce and secure drugs to deal with any public health crisis on its own terms, through its own firms.

<sup>8</sup> For other analyses on compulsory licenses issued, see Love (2007); Khor (2007), updated in (2009), among others.

could have both desirable and undesirable consequences.<sup>9</sup> A desirable consequence of such incremental innovation could be that it contributes to enhancing the technological capacity of firms and actors to produce locally adapted versions of existing products in developing countries, whether or not they are new to the world at large. This positive impact is well-acknowledged and documented by scholars of innovation studies.<sup>10</sup> However, in the context of the global pharmaceutical sector, when incremental innovations are protected by patents, they could result in the undesired effect of extending/cementing patent monopolies of firms thus making it harder for firms from developing countries to catch-up.

## **II. DEFINING THE INVENTIVE STEP IN THE PHARMACEUTICAL SECTOR: THEORETICAL AND EMPIRICAL CONSIDERATIONS**

Although the three pre-requisites of ‘novelty’, ‘industrial applicability/utility’ and ‘inventive step’ are not defined under Article 27 of the TRIPS Agreement, national patent regimes set different standards that need to be met by inventors. In order to obtain a patent, patent claims are drafted to meet these requirements in ways that set out the scope of the invention and the technological territory that is claimed to be under control in matters of infringement (Merges and Nelson, 1990). The effective coverage of a patent, that is, the patent scope, has two further dimensions to it. The horizontal scope of a patent (that is, how similar can other innovations be without infringing the original patent) determines the extent of market power that a patent confers on its owner and is etched out in the patent claim. Usually, patent claims can be drafted in ways that include, *inter alia*, a wider area of research spanning

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<sup>9</sup> This definition excludes “me too” products that are new chemical entities as well. While there is also a rise in ‘me too’ products that are not necessarily incremental innovations, in the sense that they are often different (new) molecules with similar therapeutic effects, these products are not the subject matter of this paper.

<sup>10</sup> This definition draws on insights from evolutionary economics and economics of innovation, wherein innovation consists of all processes by which firms create knowledge through use, mastery, application and adaptation of products, processes and routines that are new to them, irrespective of whether they are new to their competitors, their countries or the world at large.

beyond the invention itself. The vertical scope of the patent (also called patent height) is a function of how different a new or sequential invention must be in order to qualify for a patent, and is set out by the level of inventive step that is specified under national patent regimes.

## **II.1 Measuring the Impact of Low Patent Standards for Inventions: A Summary of Economic Arguments**

Amongst the three criteria for patentability, the implications of setting different standards of inventive step is perhaps the most difficult to analyse, generalize and measure across sectors because of its close relationship with the technologies in question, and the rate of technical change therein (Meniere, 2005). Simply put, the inventive step requires that the invention in question should not be obvious for a person having ordinary skill in the state of the art, thereby requiring a qualitative step beyond 'prior art'; a *significant* improvement. Setting the standard of inventive step determines therefore the forms of improvements of existing inventions that are patentable within a country. Although this is usually a technical specification, it remains a critical determinant of the direction of technological change within industries because it determines how individual patents can fragment a given technological field. Broadly speaking, the higher the level of inventive step, the smaller the number of patents in a given technology and the greater the scope for competition (Correa, 2008).

Specifying a lax or low level of inventive step means a proliferation of patents over a given technology, whereas specifying a rigorous standard of inventive step implies that improvements that are not significant cannot be capitalized upon through the use of patent rights. Depending on the sector in question, the uses of the invention covered by defining a low or high inventive step will vary, and the significance of these uses for future technical change will differ.

A review of the economic literature shows that arguments for and against a low level of inventive step are both used to justify policy prescriptions. It has been argued that a high inventive step precludes disclosure of essential information on the state of R&D in industries because in the absence of a patent, small inventions are not disclosed

and each inventor has to necessarily personally arrive at all the required complementary expertise to be able to get a patent. Hence low level of disclosures lead to duplicate R&D costs and can be avoided through the grant of patents based on a low inventive step (Meniere, 2005). The counter to this argument is that a low standard of inventive step is difficult for both cumulative (sequential) innovations (such as biotechnology, where disclosure of previous ‘state-of-the-art’ is important) and complementary inventions (where each invention is a step towards a new technological frontier). In both cumulative and complementary innovations, standards of inventive step not only determine how many innovative pieces of the puzzle need to fall in place for a new technology, but also how small these individual rights can be, and how they can be shared between the different inventors.

Most conventional technological domains comprise complementary inventions (Barton, 2002), within which a low standard of inventive step leads to the fragmentation of protection into smaller, individual inventions, which are all necessary to work out a technology as a whole. Such inventions are mere complements aggregated in a broader technology (Merges and Nelson, 1990). This imposes unnecessary transaction costs on the aggregated technology, and can thus slow the direction of technical change by inducing static costs as a result of scattered patents.<sup>11</sup> In the case of cumulative innovations, while low standards may result in disclosure that is important for downstream discoveries (since these are innovations that result from each other), applying such standards needs to be considered with great caution. In such cases, granting broad patent rights to the pioneering inventor is justified on the basis that it is required in order to promote the development of the technology. This however, relies on the licensing of the invention through appropriate contractual arrangements to enable other inventors to use and contribute to the growth of the technology (See Kitch, 1977; Schotchmer, 1991 and 1996). In reality, such patents can block the use of the disclosed technologies for years, unless there is a broad research exception or frequent recourse to compulsory licenses to address blocking patents as per Art 31 (l) TRIPS.

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<sup>11</sup> See US Federal Trade Commission Report (2003), that raised the same issue with regard to patent thickets.

Regardless, all these economic arguments are invariably founded on the assumption that research intensity is constantly on the rise and the inventions being patented are for the furtherance of the technological field in question.

## **II.2 Have Low Standards of Patent Protection Promoted Local Innovation Across Countries?**

In an interesting economic historical account, Chang (2002, p. 18) analyses the role played by highly interventionist industrial, trade and technology policies aimed at promoting infant industries in the catch-up processes employed by today's developed countries. He analyses the catch-up strategies employed by Britain, USA, Germany, France, Sweden, Belgium, the Netherlands and Switzerland in detail. Tracing the role of intellectual property in the catch-up process, Chang (2003) points out the importance of technology transfer, much of which was acquired through "illegitimate means" by countries from one another. His analysis highlights the following points. Firstly, by the end of the nineteenth century, the presence (or absence) of intellectual property laws within countries were key to their technology (and knowledge) accumulation strategies in general. Although the intellectual property regimes of those times were far more primitive in comparison, the lesser technologically advanced countries favoured regimes that promoted copying efforts by domestic firms, and expressly offered very inadequate protection to foreigners.<sup>12</sup> In contrast, the more technologically advanced countries sought to enact regimes that tried to prevent technological "imitation".

Economic catch up experiences of the newly industrialized countries (which jointly account for the East Asian Miracle)<sup>13</sup> as well as

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<sup>12</sup> See Chang, (2003) for a review of how patents in countries such as the USA were granted without any proof of originality, since the main aim was to acquire technologies that were key to the catch-up process. Up until 1907, Switzerland did not have an intellectual property protection regime at all, and introduced one only upon trade sanction threats from Germany. Its intellectual property laws were designed to conform to those of industrialized countries only in 1954, but chemical substances remained non-patentable subject matter until 1978 (p. 280).

<sup>13</sup> First described as the 'East Asian Miracle' by World Bank (1993) comprising Japan; South Korea, Taiwan, Hong Kong and Singapore (as the first tier Asian

the now advanced developing countries (such as India, China, South Africa) have followed a similar path. These experiences can be categorized into three stylized sets of observations. To begin with, access to knowledge and generation of knowledge locally has played a key role in economic development of countries since the eighteenth century (Mokyr, 2003). Innovation in key sectors is continuously encouraged by wide accessibility of already produced knowledge to society at low costs (Nelson, 1990; Foray, 1995). And finally, the lack of a local intellectual property regime (or of a regime that promoted the patenting of foreign inventions) has been a very important institutional mechanism historically to promote the development of local industry through promoting access to existing (external sources of) knowledge and generation of new (internal) knowledge. Such incentives have been used time and again to achieve diffusion of innovations in local environments, without restrictions on reverse engineering and copying. Especially within the pharmaceutical sector, several examples abound, including the copying of the German inventions by the Swiss until the latter half of the 1900s, and the more recent explicit promotion of reverse engineering capabilities under the Indian Patent Law of 1970.<sup>14</sup> Such regimes were premised on the need to empower local learning about the use of existing innovations, which in turn stimulated feedback improvements, enhanced local competitiveness and also promoted R&D capabilities in the long run.

The East Asian success, in particular, which has attracted much attention from the total factor productivity and structural transformation point of view, has also been accompanied by a general consensus that their ability to imitate, absorb, assimilate, replicate through ‘duplicative imitation’ was central to the transformation process (Kim, 1997; Kumar, 2002). Although intellectual property analysis is not the main focus of most economic studies of the topic, two important results can be drawn from the industrial transformation successes of these countries. A first result is that many of these countries used the policy space available to exclude or minimize intellectual property protection in ways that promoted local learning. For example, Taiwan did not have intellectual

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newly industrializing economies), and Malaysia, Thailand, and Indonesia (second tier newly industrializing economies).

<sup>14</sup> The Indian Patent Act of 1970 did not allow for product patents on pharmaceuticals and only granted process patents for a period of seven years.

property protection for sectors such as pharmaceuticals and chemicals until it was compelled to do so in 1986 (Lo, 2011). South Korea, similarly, did not recognize product patents on pharmaceuticals until the 1980s.

In some contexts, a limited amount of intellectual property, often in the form of utility model protection was used as a policy incentive to encourage local firms to invest scarce capital into reverse engineering so that technological learning ensued. However, the utility model protection in these countries was substantially different from what one observes in the case of many developed countries such as Germany.<sup>15</sup> In the East Asian economies, national laws applied a weaker standard for protection in certain cases through ‘utility models’, where a relatively lower level of novelty was accepted.<sup>16</sup> Kumar (2002) notes that in Japan, utility models protection granted a lower level of novelty. Similarly, in the context of South Korea, Kim (2003, p. 17) notes that the smaller, but smart local firms, were encouraged to reverse engineer technical knowledge embodied in products that were readily available through foreign suppliers to these firms. In Taiwan, firms were similarly attuned to local upgrading through a low local standard of novelty to such an extent that after the 1986 patent reforms, studies note that of the three forms of patents allowed in the regime – invention, new utility and new design – Taiwanese inventors took a total of 27 per cent of patents granted within the country in 2002, but most of these were still for new utility or new design, which are equivalent to process patents only (Hu and Mathews, 2005, p. 1342). In all these cases, utility models based on lower novelty requirements were a means to incentivize “...[s]maller firms that lacked both financial and technical resources, to establish their initial production facilities with primitive technologies developed by themselves, and then gradually upgraded product quality through the imitative reverse engineering of foreign products and processes.” (Kim, 2003, p. 17). In the sectors where such protection was prevalent, firms/individuals were allowed to patent the technical proficiency of

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<sup>15</sup> In Germany, for instance, the utility model protection envisages a low level of inventive step and not a low level of novelty; see Uexküll and Hölder (2006).

<sup>16</sup> See Kumar (2002) who observes this in the context of Japan and the first tier NIEs.



their product, without actually allowing any form of claims on the underlying ideas/processes.<sup>17</sup>

Despite the availability of utility models in East Asian economies, it is unclear to which extent they actually helped to cement technological progress in these countries. For instance, in an extensive analysis that compares the growth of the semi-conductor industry across USA, Japan and Korea, Shin (1996, p. 117) notes, “Although the VLSI project<sup>18</sup> produced more than 1,000 patents, they were not, in essence, technological breakthroughs, Instead, Japanese products excelled in producing better quality products through incremental innovations and the adaptation of a ‘more conservative design and a better ceramic package’”. These kinds of historical accounts seem to suggest that success was in fact due to non-patentable improvements on the underlying ideas and processes that were promoted through a wide range of industrial support infrastructure. Primarily, in addition to the absence of intellectual property protection, local firms were supported through a range of industrial policy incentives, all of which were aimed at maintaining competitiveness has much to do with upgrading technological bases in a sustained way, with an emphasis on local learning capacity.<sup>19</sup> As Hu and Mathews (2005) note, the success of the East Asian Latecomer countries “...[w]as based on building mass production systems where there was a bias towards industrial upgrading, achieved through the linkages within global value chains as well as through domestic pressures” (Hu and Mathews, 2005, p. 1329).

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<sup>17</sup> Ideas alone are not patentable, only in connection with a product or process. Competitors could thus reverse engineer the unprotected product and make it through a different/not protected process.

<sup>18</sup> The term VLSI refers to the next generation of semi-conductor computer technology. IBM’s plan to develop the large scale integration technology (VLSI) led the Japanese to plan an overtaking strategy in terms of designing a project on the same.

<sup>19</sup> See Amsden (2003), Amsden and Chu (2005), Amsden (2005), among others.

### II.3 The Global Reconfiguration of Pharmaceutical Innovation and Changing Patenting Standards

Reichman (2000, p. 1748) rightly notes that the trend towards a lax inventive step promoting the patenting of incremental innovations has been prompted by the fear that patentable information will be subject to “slavish imitation” before the lead-time advantages of being the inventor can be realized. The pharmaceutical sector is a glowing exemplar of this. Having relied historically on the organized exploitation of research and development activities, wherein upstream open science is conducted in public sector laboratories, research institutes, universities and teaching hospitals; and commercial innovation is largely the domain of the ‘big pharma’ (Kaplan, 2004; Cockburn, 2004), the global regulatory system has for a long time structured itself around the needs of the ‘big pharma’. Patent protection in the pharmaceutical sector has found repeated justification on the basis that drug discovery and development required large scale investments, uptake of significant risks, time spans ranging between ten and fifteen years, but could be copied at marginal expense. Patents therefore were essential to provide incentives to private firms.

This argument simply found a renewed and stronger emphasis when the sector was under pressure to deliver profitable new drugs in the 1990s, which resulted in a series of global mergers and acquisitions amongst global pharmaceutical firms that focused exclusively on enhancing in-house productivity of R&D (CIPHI, 2006). Between 1985 and 2005, there were at least 50 mergers and acquisitions worldwide, leading to a more concentrated pharmaceutical industry at the global level (Boldrin and Levine, 2008; Smith et al, 2009). Three discernable trends accompanied this shift:

1. Acceptance of lax patenting criteria for pharmaceutical products: The wider landscape of patenting was gradually shifting from inventive activity interpreted as notions of “flash of creative genius”<sup>20</sup> or “a function never before performed, a wholly novel device or one of such novelty

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<sup>20</sup> *KSR International Co vs. Teleflex Inc.*, 550 U.S. 127 S. Ct. 1727. A similar ruling was made in 1851 Supreme Court decision of *Hotchkiss vs. Greenwood*, 52 U.S. (11 How.) 248 (1851).

and importance as to mark a distinct step in the progress of art”,<sup>21</sup> which were commonly placed demands for the grant of patents over the last two centuries globally. The grant of a patent, more generally, was no longer for generation of information over a technology, but rather for the generation of scientific information that pertains to methods of processing or producing an output simply conferring commercial advantages to the person who possesses the information (Reichman, 2000, p. 1750).

2. The surge in incremental innovations: Against the backdrop of a shifting emphasis in patenting and difficulties in discovering new chemical entities, the focus of a large share of patenting in the sector has turned away from new chemical entities towards a range of incremental innovations. Kortum and Lerner, in an analysis of trends in US patenting note as early as 1998 that there was a surge in patenting across a broad spectrum of technologies which was not explained by the new technological opportunities arising out of software, biotechnology and related fields. Their analysis further found that the increase in patenting was not accompanied by a proportionate increase in R&D spending, leading them to conclude that when compared to earlier periods in history, the patent system is beginning to be heavily exploited by patentees. They further note that whereas research intensity rose rapidly in the 1980s, it flattened in the 1990s although patenting continued to surge (Kortum and Lerner, 1998, p. 286).
3. An emphasis on evergreening: A reason behind the rise in patenting, at least in the pharmaceutical sector, can be attributed to the growing emphasis on evergreening; a term that refers to the numerous ways in which pharmaceutical firms routinely use the patent system to extend protection over their molecules using various ‘life management techniques’.<sup>22</sup> According to estimates, no more than a third of all drugs patented in the USA have therapeutic benefits

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<sup>21</sup> *Westinghouse vs. Boyden Power Brake Co.*, 170 U.S. 537, 561-62 (1898).

<sup>22</sup> Other reasons, such as the importance of patents as strategic assets in licensing, use of patents for prevention of competition in new research areas, are all also important here.

over existing drugs, signifying the uncanny rise of patents with no innovative content at all or are at best incremental innovations.<sup>23</sup> Common ways of accomplishing such an extension is through patenting an analogue or crystalline or other form of the molecule whose patent is about to expire, or packaging two molecules whose patents are about to expire, or embedding drug brands in intricate clusters of patents that make patent disputes costly.<sup>24</sup> Estimations based on patent statistics in the EU show that there is usually a tendency to hugely cluster patents claiming all uses around the first patent that are about to expire in order to delay the entry of generics.<sup>25</sup> On the same point, the NIHCM notes as early as 2002 that two thirds of all drugs granted patents between 1989 and 2000 in the USA contained active pharmaceutical ingredients that were already in the market. Patent litigation trends in the USA further show that the courts usually hold somewhere between 45-55 per cent of all litigated drug patents invalid (NIHCM, 2002). Similarly, between 2000 and 2007, generic producers prevailed in 62 per cent of the final judgments rendered by European courts in pharmaceutical patent litigation cases between originator and generic companies (EC, 2009, p. 12).

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<sup>23</sup> Boldrin and Levine (2008), p. 226. This figure does not make a distinction between incremental innovations and 'me too' products.

<sup>24</sup> Loefgren (2007), p. 3. Technically speaking, the new patent on the modified substance does not prevent the use of the original substance for which the earlier patent has expired. The new patent only encompasses the new version of the molecule, or the combination package of molecules. But in practice, it is difficult for the competitor or a judge to distinguish the scopes of the original and the new patent, which enables patent holders to engage in abusive litigation, i.e. injunctions to stop the generic producer from using the original substance. New uses of the same substance are different from these structural modifications; here the new patent covers exactly the same substance as the original patent (but for a different use).

<sup>25</sup> See <http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/si.pdf>.

### **III. IMPLICATIONS OF LAX PATENTING CRITERIA ON DEVELOPING LOCAL PRODUCTION AND INNOVATION CAPACITY IN DEVELOPING COUNTRIES**

The emerging trends in the pharmaceutical sector as a result of low standards of inventive step carry with them not only general concerns on the nature and direction of technological change, but also a far more urgent issue, that is, how do lax patenting standards impact public health. This issue calls for an assessment from two different perspectives. Is a lax definition of inventive step in the interest of local pharmaceutical firms in developing countries? Are there other possible implications of lax patenting criteria on access to medicines and public health that developing countries need to be mindful of? Both issues are discussed here.

#### **III.1 Technological Learning, Local Production and Innovation in the Pharmaceutical Sector**

Pharmaceutical production (and eventually innovation) is quite different even within developing countries. While generally speaking, it is not the domain of small and medium enterprises in developing and least developed countries, large firms in least developed countries engaged in pharmaceutical production tend to be much smaller in size (measured in terms of both, the number of people employed and net annual turnover).<sup>26</sup> Furthermore, a distinction needs to be made between small and medium enterprises that thrive and perform in niche areas such as biotechnology and genomics in the more advanced developing countries from pharmaceutical firms struggling to build capacity in most other developing and least developed countries.

Table 1 presents a quick typology of pharmaceutical production and innovation capabilities in developing countries.

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<sup>26</sup> For instance, the largest pharmaceutical firms in Uganda or Ethiopia are of a much smaller size than those in India or Brazil.

Table 1

**A typology of pharmaceutical innovation capabilities**

<b>Capabilities</b>	<b>Institutional basis for learning and innovation</b>	<b>Some examples<sup>27</sup></b>
No skills	Fragmented basis for innovation, lacking human skills and knowledge infrastructure, lack of policy focus on health innovation.	
Manufacturing activities	Incremental innovation based on large-scale reverse engineering skills, evidence of clear strengths in either API formulations or assembling medicines in pills, tablets or other dosage forms by importing the APIs required, commensurate human skills, policy emphasis on local production.	Kenya, Uganda, Tanzania, Nigeria, Ethiopia
Reverse engineering for APIs, incremental innovations in generics, some drug R&D	Learning mainly through reverse engineering activities, persistence of at least some international collaboration, a resilient local generics sector and presence of local demand to sustain production activities, policy vision/ emphasis to promote local production.	South Africa, Bangladesh
Drug and vaccine R&D, niche specializations in biotechnology, biologics, etc.	Gradual technological upgrading visible across the sector, capacity to perform R&D in both private and public sector institutions, availability of competent human skills and knowledge infrastructure, policy emphasis on knowledge creation and presence of secondary instruments such as IPRs, venture capital and other dedicated measures.	India, China, Brazil

Source: Gehl Sampath, 2010.

<sup>27</sup> There are several other countries that can be grouped under these categories; this column only contains some examples.

The important common factor that runs through all developing countries that have managed to set up pharmaceutical sectors is the extensive investment (in terms of physical infrastructure, scientific infrastructure as well as finances) that was required to set up firms (whether government owned or private) to foster local pharmaceutical capacity to produce drugs and related products. Such products, although not new to the world or science at large, have been a significant step towards the creation of independent local pharmaceutical enterprise in developing countries; a backbone of industrial activity. Empirical data on how countries build pharmaceutical production and innovation capacity shows that access to knowledge that forms the basis of generic production needs to be provided for, within a suitable environment that supports industrial development along with sufficient investments in physical and scientific capital that is required for expansion of the local firms.

Experiences of countries, even the more recent countries in the Asian and African context call attention to the role of the state and public sector institutions in providing key industry infrastructure, such as standardization and testing, production of active pharmaceutical ingredients, quality control and quality testing, clinical services, biotechnology, among many others. These common industry infrastructures seem to play a very important role in enabling firms to produce generic formulations of existing drugs in the first place, and also to move up from low-value production to higher value production firms with a simultaneous shift in incremental innovation capacities. Furthermore, experiences of countries such as India and China lend strength to conclusions similar in the case of the East Asian Miracle, that expanding indigenous technological capability has been a result of an overarching emphasis on reverse engineering and their relentless effort to acquire technology from outside.

Local firms engaged in pharmaceutical production are mostly those that provide generic versions of already established drugs in developing country markets (for local consumption and through exports to other developing and least developed countries). More often than not, developing such production capacity and pursuing products that are often either the subject matter of existing patents abroad, patent extensions and evergreening efforts by international firms requires

substantial investments by local companies in terms of discovering new ways of producing the same product (in case of process patents), or producing a new variation of the product (in case of product patent) or even just arriving at the same product through a locally efficient process. Economies of scale and scope go a long way in this process to offset the risks incurred by the local firms to engage in production.

In the pharmaceutical sector, low patenting standards can have two different, equally detrimental impacts. First and foremost, a low inventive step is prone to abuses, leading to extension of patent monopolies through products embodying very minor changes. There is no basis to assume that such a lower technical requirement would be in favour of developing local production and innovation capacity in developing countries. A lax inventive step allows the grant of patents that extend existing monopolies and guarantee markets for international firms in developing countries, thus making it harder for local firms to overcome constraints. In other words, this would mean that all those variations of the patented product developed by local firms that are very close to the original product will be considered as equivalent to the original and thus an infringement of the patent. More importantly, given the sectoral dynamics of learning, it is unclear how granting patents that fragment and limit access to underlying processes and products in the pharmaceutical sector will add value. As early as 1990, Merges and Nelson captured the different ways in which technical advances proceed in different fields to show that "...[t]he issues at stake regarding patent scope depend on the nature of technology in an industry". Decisions on the level of inventive step need to be taken according to the sector in question, precisely because it affects the development of technology both in terms of individual inventions and future improvements that are allowed and can be built upon (Merges and Nelson, 1990, p. 843).

Second, it can, as has been argued, lead to overly fragmented technology domains, for example, patenting of genetic sequences, and medical tools and platforms. Fragmenting inventions on this basis can lead to difficulties in conducting downstream research (since each patent holder may choose to supply his/ her input only at a high cost), putting the profitability of the entire R&D venture at stake (Heller and Eisenberg, 1998; Denicolo, 2007). The flow of ideas, skills and research tools within the technological domain are hindered by transaction costs



arising due to institutional heterogeneity and conflicting agendas of the different agents, difficulties in valuation of tools and associated information and increased litigation.<sup>28</sup> Research tool users feel that the provider is asking for too much in return for access to a patented product based on an over-valuation of the contribution of the tool relative to other inputs for future valuable discoveries. Such factors create situations that increase costs of bargaining for research tools and hinder meaningful exchange; and rather seem to point out to how patents can be used strategically to block research.<sup>29</sup> As Cohen et al (2000) appropriately note: “Patents become weapons in mutually reinforcing, non-cooperative strategic interactions where firms feel increasingly compelled to patent either because they need to protect themselves from suits or from being blocked, or they want to block rivals or use patents as bargaining chips in negotiations.” The transaction costs of such patents that fragment a given technology can go well beyond bargaining, into specific forms of commercialization hurdles (OECD, 2002). Patent thickets and royalty stacking often occur, and discourage subsequent innovators – the larger the number of licenses that have clauses on royalty sharing on the final product, the lower the revenue for the innovator.<sup>30,31</sup> These are also undesirable impacts from the perspective of promoting learning and technological change in developing countries.

From a social policy perspective, the objective of an innovation-oriented patent regime in a developing country context would be to promote competition amongst local firms (and also between local and foreign firms) in order to ensure the availability and affordability of drugs within a balanced and supportive framework. **Given the**

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<sup>28</sup> See Eisenberg (2001) and OECD (2002), among others. Eisenberg summarizes these as the main issues that were significant during the investigation of the Working Group on Research Tools, National Institute of Health, USA, 1998, which investigated difficulties encountered by researchers in obtaining access to proprietary research tools in biomedical research.

<sup>29</sup> See also Grandstrand (2000) in this context.

<sup>30</sup> Royalty stacking refers to a situation where each earlier innovator grants access to his/her product in return for a royalty on the new innovation. The greater number of earlier patents that need to be licensed to proceed with innovation, the larger the number of royalty agreements that get “stacked” on to the yet-to-be-discovered product.

<sup>31</sup> See EPO (2007) on the increasingly cumulative nature of innovation and the effect of blocking patent thickets.

**particular features of the pharmaceutical sector and the evidence on the impact of a lax inventive step analysed here, the interest of building local capacity is better achieved in a regime based on rigorous patentability criteria.** Setting a high inventive step will help prevent the strategic use of patents by multinational companies to block the generic industry in developing countries. Such grants of patents lead to costly litigation and may not even be effective since generic firms seeking to revoke the patent need to litigate in each and every jurisdiction where the patent has been issued on frivolous grounds.

In the case of some developing countries with a good level of production capacity (such as India), patenting incremental innovations can be as lucrative an option for the generics industry as for the global "big pharma". In fact, evidence collected in an earlier field study of the Indian pharmaceutical sector in 2008 points towards a tendency wherein generic firms could themselves engage in extensive incremental patenting in a bid to either fence off patent applications to themselves, or to pre-empt patent thickets from competition (field interviews, Cipla and Aurobindo pharmaceuticals). Specifically, an important distinction was observable in the patenting behaviour of Indian firms: while Indian firms were not allowed to patent incremental innovations within the country as a result of Section 3(d) of the Indian Patent Act,<sup>32</sup> their patenting behaviour abroad (especially in the US) was very similar to that of their international competitors. In several cases, the firms interviewed were also of the view that patents helped them in out-of-court settlements with the global pharma by serving as strategic assets to bargain in the generics sector (Gehl Sampath, 2008).

While it is clear that more data is needed to draw concrete conclusions on the subject, the information gathered nevertheless points out that a lax level of inventive step could be used by local generic firms and multinational companies alike to promote the proliferation of patents on incremental uses, thereby fostering non-dynamic forms of competition in the local market (where firms compete for market shares, fragmenting the pie by cutting into each other's profits) and undercutting the cause of public health.

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<sup>32</sup> See discussion on Section 3(d) of the Indian Patent Act in Box 2 of this paper.

### **III.2 Other Detrimental Implications of a Lax Inventive Step: Some Preliminary Findings on Compulsory Licensing and Access to Medicines**

A further impact of a lax inventive step would be the unnecessary patenting of incremental innovations that impede the cause of public health, calling for the issuance of compulsory licenses on drugs of importance to public health. Of the various flexibilities contained in the TRIPS Agreement, compulsory licensing has been perhaps the most politically contested and practically difficult to implement. Part of the difficulties in implementing the provision have stemmed from the inability of several countries to domestically manufacture. In order to ease the way for such countries, newer institutional mechanisms were created under Paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health and the 30 August 2003 decision of the WTO, that allowed for other countries (both developed and developing) to produce generic drugs for export to any developing or least developed country lacking the local manufacturing capacity. Over the past years, several developing countries have issued compulsory licenses (CLs) or used the 'government use' provision to produce drugs of importance to public health locally. Table 2 contains a list of countries, along with other details such as drug price reductions, remuneration offered to patent holder firm and the type of license issued.

Table 2

#### **Compulsory Licenses/Government Use Options Exercised by Developing countries**

<b>Date/ Country</b>	<b>Reasons</b>	<b>Type of license</b>	<b>Impact on drug prices</b>
May 2002 Zimbabwe	HIV/AIDS	CL to a local generic company Varichem Pharmaceutical Co. to produce seven generic versions of first line ARVs	Prices of the locally produced drugs are determined by the Minister and based on price control mechanisms.

Date/ Country	Reasons	Type of license	Impact on drug prices
November 2003 Malaysia <sup>33</sup>	HIV/AIDS	CL to import generic version of ARVs from Cipla (India) for 2 years beginning on 1 November 2003	The ceiling price for the said drugs to be supplied to the Ministry of Health, Malaysia shall not exceed the following: (a) Didanosine 100 mg tablet – RM74.58 (per box of 60 tablets) (b) Didanosine 25 mg tablet - RM22.80 (per box of 60 tablets) (c) Zidovudine 100 mg capsules - RM5.89 (one set of 10 capsules) (d) Lamivudine 150mg + Zidovudine 300mg tablet – RM153.50 (per box of 60 tablets)
April 2004 Mozambique <sup>34</sup>	National emergency and extreme	CL to Pharco Mozambique Ltd. for local	

<sup>33</sup> See CP Tech website: <http://www.cptech.org/ip/health/c/malaysia/arv-license.html>. Also documents showing Authorisation for exploitation of patented invention in Malaysia By virtue of Section 84(1)(a), Patents Act 1983, Syarikat Megah Pharma & Vaccines (M) Sdn Bhd (Company No: 552048-H). Also see Ling (2006).

<sup>34</sup> See CP Tech website: <http://www.cptech.org/ip/health/c/mozambique/moz-cl-en.pdf>. English translation of the Ministry of Mozambique Compulsory License No 01/MIC/04.

<b>Date/ Country</b>	<b>Reasons</b>	<b>Type of license</b>	<b>Impact on drug prices</b>
	urgency (HIV/AIDS)	manufacture of the mentioned triple compound under the names of PHARCOVIR 30 and PHARCOVIR 40	
September 2004 Zambia <sup>35</sup>	National emergency and extreme urgency (HIV/AIDS)	CL to Pharco Ltd., a local producer, for production of triple fixed-dose combination.	
October 2004 Indonesia <sup>36</sup>	Presidential Decree No 83 of 2004 Regarding Exploitation of Patent by the Government on Antiretroviral Drugs for Government use	CL of Minister of Health to appoint a “pharmaceutical factory” as the patent exploiter on behalf of the Government	Price differential between patented and generic drugs are substantial
June 2005 Eritrea <sup>37</sup>	National emergency (HIV/AIDS)	CL for import of generic ARVs	

<sup>35</sup> See CP Tech website: <http://www.cptech.org/ip/health/c/zambia/zcl.html>.

<sup>36</sup> Ministry of Commerce, Trade and Industry letter, Compulsory Licence No.01/2004, signed by Minister Patel, 21 September 2004 and please see TWN website: <http://www.twinside.org.sg/title2/par/TRIPS.flexibilities.30jan07>.

<sup>37</sup> See CP Tech website: <http://www.cptech.org/ip/health/cl/Eritrea.png>.

<b>Date/ Country</b>	<b>Reasons</b>	<b>Type of license</b>	<b>Impact on drug prices</b>
October 2005 Ghana	HIV/AIDS	CL to import Indian generic HIV-AIDS medicine <sup>38</sup>	ARV costs dropped almost 50 per cent from \$495 per year to \$235 per year per patient <sup>39</sup>
November 2006 Thailand	Government Use effective up until 31 December 2011	CL to import Indian generic and locally produce Efavirenz. The amount to not be more than 200,000 patients per year, for those covered under the National Health Security System Act B.E.2545, Social Security Act B.E. 2533, and the Civil Servants and government employees' medical benefits scheme.	Merck retained the marketing licence rights in Thailand and charges 1,500 baht per month (US\$41).  Thailand imported a generic version of the drug from India, at an estimated cost of 800 baht per month per person. <sup>40</sup>
January 2007 Thailand	Government use effective up until the patent expired or no	CL for the heart disease drug Plavix (Clopidogrel bisulphate).	The cost of Plavix was expected to drop from 120 baht per pill to 6-12 baht per pill. <sup>42</sup>

<sup>38</sup> James Love (2007).

<sup>39</sup> Khor (2007), p. 10.

<sup>40</sup> See CP Tech website: <http://www.cptech.org/ip/health/c/thailand/>.

<sup>42</sup> Khor (2009), p. 9.

<b>Date/ Country</b>	<b>Reasons</b>	<b>Type of license</b>	<b>Impact on drug prices</b>
	essential need.	Allowing the provision of generic drugs of Clopidogrel is unlimited for patients covered under the National Health Security Act B.E.2545, Social Security Act B.E.2533 and Civil Servants and Government Employees Medical Benefit Scheme but is under doctors' judgment. <sup>41</sup>	
January 2007 Thailand	Government use of the patent rights are effective until 31 January 2012	CL for the AIDS drug Kaletra (LPV+RTV). The use of the patent rights will be limited to the provision of Efavirenz to not more than 50,000 patients per year, for those covered	In 2007, 6000 Baht per month or 72,000 Baht per year per patient charged by Abbott Lab. Expect generic version to be 20 per cent less. <sup>43</sup>

<sup>41</sup> See CP Tech website: <http://www.cptech.org/ip/health/c/thailand/>.

<sup>43</sup> The Ministry of Public Health and The National Health Security Office Thailand, 'Facts and Evidences on the 10 Burning Issues related to the Government Use of Patents on Three Patented Essential Drugs in Thailand, Document to Support Strengthening of Social Wisdom on the Issue of Drug Patent,' February 2007, ISBN 978-974-94591-5-7.

Date/ Country	Reasons	Type of license	Impact on drug prices
		under the National Health Security System Act B.E. 2545, Social Security Act B.E. 2533, and the Civil Servants and government employee's medical benefits scheme.	
May 2007 Brazil	Government use after negotiations with patent holder broke down.	CL to import generic efavirenz from India rather than buy Stocrin – the brand name for patented efavirenz – from its US-based manufacturer Merck & Co.	Brazil issued compulsory license for efavirenz to be imported at US\$ 0.46 per pill. <sup>44</sup>
November 2009 Ecuador	A matter of public interest	CL was issued by the national Ecuadorian Institute of Intellectual Property (IEPI), and the term of application of the license is until 14 November 2014	The CL reduced the cost of a major HIV drug by 27 per cent, and prices were expected to drop much further.  Kaletra (costing \$1,000 annually per person) was

<sup>44</sup> Johanna von Braun, 'Use of Compulsory Licenses Selected National Experiences', IP Law and Policy Research Unit, University of Cape Town. Available from [http://www.unctad.org/sections/dite\\_totip/docs/tot\\_ip\\_0018\\_en.pdf](http://www.unctad.org/sections/dite_totip/docs/tot_ip_0018_en.pdf).



Date/ Country	Reasons	Type of license	Impact on drug prices
		for ritonavir. It was granted on 14 April to Eskegroup SA, a Latin American distributor headquartered in Guayaquil for CIPLA, a leading Indian generic drug producer.	available at \$800 under the CL. Prices were expected to continue to fall as the government licensed more competitors. <sup>45</sup>

*Source:* Compiled by author from various sources.

A closer analysis of the reasons and results of CLs issued in countries lends strength to a few interesting results.

### ***III.2.1 The Political Economy of CLs***

To begin with, the use of CL has resulted in substantial price reductions in the countries that have used them, and by implication, improved access to medicines. Despite this, the examples of developing and least developed countries resorting to CL have been few and far between.

Comparing countries on their relative policy positions in choosing CL reveals some interesting insights. To begin with, from a political economy perspective, all countries that did choose the option were big developing countries and had some demonstrated ability to engage in local pharmaceutical production or were obliged (as in the case of Brazil, through a constitutional provision) to ensure affordable access to medicines. The policy choices therefore seem to be dictated from a dual perspective of promoting public health through local production, supported by the ability to withstand international pressure.<sup>46</sup> A second interesting aspect concerns the general industrial

<sup>45</sup> People's Health Movement, 'Praise for grant of CL for AIDS drug', 4 May 2010. Available from <http://www.phmovement.org/en/node/2883>.

<sup>46</sup> The compulsory licenses in both Brazil and Thailand demonstrate this fact.

environment for pharmaceutical production and innovation in these countries. Developing and least developed countries choosing to implement the CL option are already those with restrictive policies for investment of foreign firms, their terms of engagement, and pricing (see the discussion below in the case of Indonesia, for example) or those with extremely low levels of FDI and global pharmaceutical activity within their national frontiers (Zimbabwe and Eritrea for example). In this context, although unclear, there seems to be a general apprehension that the grant of CL in countries would result in a reduction of other potential positive effects of granting pharmaceutical patent protection, namely, FDI into the sector and innovative presence of pharmaceutical firms (see box 1).

Box 1

**Compulsory Licences and Foreign Direct Investment**

Can under certain circumstances, the existence of effective mechanisms for compulsory license/government use and the political will of a government to effectively apply them, induce patent holders to set or negotiate reasonable conditions for access to protected products, without affecting their innovative efforts nor foreign direct investment or the commercialization of new products in the countries where such mechanisms are applied? It remains unclear as to whether extensive use of CL does diminish other so-called incentives of offering patent protection for example, FDI, introduction of new products and innovative presence of global firms. Empirical evidence on each of these aspects is contested but points towards a general tendency that simply granting IPRs on pharmaceutical products and refraining from using TRIPS flexibilities is no guarantee of greater FDI/foreign innovative activity in the sector.<sup>47</sup> A recent example of a

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<sup>47</sup> More generally, although FDI remains an important mode of technology, FDI in productive sectors of the economy depends on structural conditions for trade and technology within the country (see Hoekman, Maskus and Saggi, 2005). In the case of countries that show a low technological capacity and innovation infrastructure, intellectual property reforms alone do not lead to greater FDI. Also, most FDI remains to be continuously directed at extractive industries amongst least developed countries (UNCTAD 2007). In this context, Mendi (2007) notes that license fee

country that sought to promote FDI in the pharmaceutical sector through a joint venture with a well-known international generic firm is Uganda. The Cipla Pharmaceuticals-Quality Chemicals venture that was set up in 2008 is a unique example of a joint venture supported extensively by the government of Uganda in order to promote FDI in the pharmaceutical sector. In this case, the government chose to promote the joint venture, with Cipla granting licenses for some ARVs and anti-malarial drugs and tacit know-how and training to Quality Chemicals, in return for a 50 per cent share in all profits. The government has committed to purchase the products of the joint venture for the first several years (UNCTAD, 2011a).

*Source:* Compiled by author from various sources.

### ***III.2.2 CLs and a Rigorous Inventive Step***

Some of the CLs that were issued by the bigger developing countries could have been avoided if countries had clearly defined a rigorous inventive step. Table 3 contains a list of products that have secured patents in developing countries as a result of a lax inventive step and then have been the subject of compulsory licenses, due to the negative implications of the grant of the patents on access to medicines.

For instance, in the case of Thailand, the compulsory license could perhaps have been avoided if Thailand had used a more rigorous standard for patentability for ritonavir, as witnessed in the Indian patent regime. The compulsory license has then however, been issued to deal with the public health impact of the patent. While the list in table 3 and the examples given thereafter are merely illustrative, it indicates the importance of a rigorous inventive step in the interest of public health.

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payments are mostly associated with the presence of multinational companies in the country and most technology is received by subsidiaries.

Table 3

**Incremental Innovations and Compulsory Licensing**

<b>Product background</b>	<b>Efforts to issue compulsory licenses for reasons of public health<sup>48</sup></b>
AZT and lamivudine (Combivir) Patent held by GlaxoSmithKline (GB2235627), a combination of its earlier two ARV products, AZT (patent expiry date 2005) and lamivudine (patent expiry date 2007).	Malaysia Ecuador
Lopinavir/ritonavir (Kaletra) Abbott has filed at least 75 patents on various versions of lopinavir/ritonavir. <sup>49</sup> Most recently, a patent for the soft gel capsule form of ritonavir (brand name Norvir) was rejected in India. <sup>50</sup>	Thailand (issued for lopinavir and ritonavir)
Nevirapine An aqueous suspension of the hemihydrate form of nevirapine is patent protected (Nevirapine Hemihydrate) apart from other pending applications on different forms of the drug.	Zambia
Oseltamivir (Tamiflu) There are at least two patents on the compound oseltamivir and its salts/esters <sup>51</sup>	Argentina Canada

*Source:* Compiled by author from various sources.

<sup>48</sup> This column lists the countries that sought to compulsory licensing, irrespective of whether or not the license was eventually issued. A complete list of countries that have used the compulsory license option is discussed in the section 4 of the paper.

<sup>49</sup> I-MAK reports, available from <http://www.i-mak.org/lopinavirritonavir/>. Accessed on 14 January 2011.

<sup>50</sup> New York Times, India Rejects Sham Patent Application for Lifesaving HIV Drug: Pharmaceuticals in India now free to help HIV patients worldwide. 2 January 2011. New York, NY.

<sup>51</sup> (Basheer and Amin, 2006).

It remains questionable to what extent smaller developing countries can resort to the option of issuing CLs to promote access to medicines locally, as done by some of the bigger countries. Stipulating a rigorous inventive step, therefore, is an ex-ante measure that will help prevent the abuse of the patent system and public health goals by patent holders, circumventing a situation where unnecessary political capital is required by countries for the issuance of CLs as an afterthought. A rigorous inventive step in the Indian Patent Regime (see box 2) is an interesting example of how the patenting of incremental innovations can be contested (and avoided) in the interest of public health.

**Box 2****Example of a Rigorous Inventive Step: The Indian Patent Regime**

The case of the Indian patent regime serves as a very good example, wherein a rigorous requirement for inventive step has been defined under Section 3(d) of the new Indian Patent (Amendments) Act of 2005 that brought the Indian patent regime into full compliance with the TRIPS Agreement. Section 3 (d) specifies that patents will not be granted automatically for different forms of the same molecules, such as salts, esters, polymorphs and decisions will be taken case-by-case to establish the standard of inventive step in an effort to prevent ever-greening of molecules. Section 3(d) was challenged by Novartis in the Chennai High Court in the case of Glivec, and was held by the Chennai court to be constitutional and not against the TRIPS Agreement.<sup>52</sup> Two particular contentions formed the core of the

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<sup>52</sup> Glivec, Novartis's anti-cancer drug, was India's first exclusive marketing right (EMR), on a beta crystalline version of the compound Imatinib Mesylate. Indian generic producers of the drug challenged the EMR on grounds that the compound Imatinib Mesylate was a derivative of a molecule that was known prior to 1995, and therefore does not qualify for patent protection. At the time when the EMR was granted, several Indian companies were producing generic versions of Imatinib Mesylate, including, Cipla, Ranbaxy and Sun Pharmaceuticals. The EMR was withdrawn and Novartis was subsequently also refused a patent on Glivec. In response, Novartis moved the Indian high court challenging the constitutional validity of section 3 (d) in the Indian Patent Act of 2005, claiming that such a stipulation is against the TRIPS Agreement. The High Court in Madras issued a

case. First, the constitutionality of the provision and its conformity with TRIPS and a second contention related to the correct application of Section 3(d) to the particular case by the patent office. While the first was settled by the Chennai High Court, the second issue was addressed by India's IP Appellate Board (IPAB). The latter confirmed the patent office's rejection of a patent for Glivec, denying "significantly enhanced efficacy" of Glivec under Article 3(d) over a previously known molecule. Following the IPAB decision, Novartis has appealed to India's Supreme Court (UNCTAD, 2011b). Despite this, the first decision upholding the validity of section 3(d) and the facility of pre-grant oppositions contained in the Indian patent regime have helped to contest the grant of patents on ever-greened products to a very large extent within India.

As a result of the rigorous inventive step definition contained in the Indian patent regime, several other compounds that are of importance to public health and have been contested including:<sup>53</sup>

- a. tenofovir disoproxil fumarate (Viread) used for the treatment of HIV<sup>54</sup>;
- b. an ester derivate of tenofovir disoproxil for the treatment of HIV<sup>55</sup>;
- c. a pseudopolymorphic form of darunavir (Prezista) used for the treatment of HIV<sup>56</sup>;
- d. Nevirapine Hemihydrate, an aqueous suspension of the drug Nevirapine, used for the treatment of HIV in children;
- e. Gilead's patent on a combination treatment for HIV

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judgment in 2007, deeming Section 3 (d) to be constitutional and not against the TRIPS Agreement.

<sup>53</sup> All the examples listed here have been contested in India following section 3(d) of the Indian Patent regime.

<sup>54</sup> Pre-grant opposition in India, Gilead Sciences Inc. (application no. 896/DEL/2002) vs. Intermed labs Pvt Ltd, Delhi Patent Office (2009). Also see Gilead Sciences Inc. (application no. 896/DEL/20020 vs. Cipla Ltd, Delhi Patent Office (2009).

<sup>55</sup> Pre-grant opposition in India, Gilead Sciences Inc. (application no. 2076/DEL/1997) vs. Cipla Ltd, Delhi Patent Office (2009).

<sup>56</sup> Pre-grant opposition in India, Tibotec Pharmaceuticals Ltd (application no. 3598/DLNP/2004) vs. Cipla Ltd, Delhi Patent Office.

comprising tenofovir disoproxil fumarate (Viread) and emtricitabine (emtriva);<sup>57</sup>

- f. Crystalline form of adefovir dipivoxil (Hepsera) and other compositions used for the treatment of Hepatitis B.<sup>58</sup>

The illustrations above can be expanded to include numerous other examples of patents on drugs used to treat cancer, arthritis and other such diseases.<sup>59</sup>

### ***III.2.3 Promoting Local Production Capacity***

Defining a rigorous inventive step is also important for developing countries not only from the perspective of access to medicines, but also to promote local production and innovation capacity, as opposed to importing drugs through CLs. Even here, some important distinctions can be deciphered from the country experiences, which although not conclusive are indicative of these differences. Malaysia issued a government use exception for the import of ARVs from the Indian generic firm, Cipla Pharmaceuticals. Malaysia has a relatively low emphasis on the local production of pharmaceuticals. In the case of Indonesia, which has an emphasis on local production,<sup>60</sup> the government use exception was used to authorize a local government company, Kimea Pharmaceuticals to produce drugs. Except for Thailand, the other countries have largely been one-time users of the mechanism.<sup>61</sup> In the African countries, while Zimbabwe and Zambia both issued CLs for production to local generic firms in the country, Ghana and Eritrea both issued CLs for import of generic ARVs from Indian firms.<sup>62</sup> In some of

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<sup>57</sup> Pre-grant opposition in India, Gilead Sciences Inc. (application No. 3383/DELNP/2005) vs. Cipla Ltd, Delhi Patent Office (2009).

<sup>58</sup> Pre-grant opposition in India, Gilead Sciences Inc. (application No. 712/DEL/2002) vs. Ranbaxy Laboratories, Delhi Patent Office (2009).

<sup>59</sup> See for example, <http://www.i-mak.org/pharma-patent-decisions/>.

<sup>60</sup> See UNCTAD study (2011).

<sup>61</sup> This is also because in most cases, the patent holder firms have been keen on reducing the prices of drugs pursuant to threat of CL, rather than to allow competitive manufacturing.

<sup>62</sup> In the case of Eritrea, it is not clear if the CL was issued to import from an Indian firm. More generally, the information on African countries is scant.

the smaller African countries, there is also an issue of local public acceptance of the products produced through CL, which could be dealt with more effectively if done within a general broader framework that seeks to promote local production capacity and promote consumer trust in locally produced medicines.<sup>63</sup>

In this context, most evidence from developing countries that have some capacity to engage in the pharmaceutical sector (through reverse engineering and formulations) shows that the limiting of patenting and, by implication, of the presence of foreign firms, was an important trigger for the growth of the local sector. Examples abound, of which three cases can be mentioned here as interesting evidence. In the case of Bangladesh, the National Drug Policy of 1982 has sought to limit the presence of foreign firms as well as foreign drug products sold in the local market to only those categories that are not manufactured by the local firms. As a result of this policy, local firms that supplied to less than 15 per cent of the local market in 1982, supply now to over 85 per cent of the total market in 2010. In Indonesia an earlier policy regime that required that foreign pharmaceutical firms set up local factories in order to be able to sell their products in the local market was strengthened by a new Decree 1010 issued by the Indonesian Ministry of Health in late 2008. The decree requires every company to manufacture every one of its pharmaceutical products in Indonesia,

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<sup>63</sup> For example, in the case of Mozambique, research shows that patients prefer patented ARVs over the generics produced locally. See Russo and McPake (2009). This research investigates medicine prices in urban Mozambique with the objective of understanding how prices are formed and with what public health implications. The study adopts an economic framework and uses a combination of quantitative and qualitative methods to analyse local pharmaceutical prices and markets. The research findings suggest that: (a) local mark-ups are responsible for up to two-thirds of drugs' final prices in private pharmacies; (b) statutory profit and cost ceilings are applied unevenly, due to lack of government control and collusion among suppliers; and (c) the local market appears to respond effectively to the urban population's diverse needs through its low-cost and high-cost segments, although uncertainty around the quality of generics may be inducing consumers to purchase less affordable drugs. We conclude that local markets play a larger than expected role in the determination of prices in Mozambique, and that more research is needed to address the complex issue of affordability of medicines in low-income countries. We also argue that price controls may not be the most effective way to influence access to medicines in low-income countries, and managing demand and supply towards cheaper effective drugs appears a more suitable policy option.



failing which their product licenses will be withdrawn, rendering them unable to sell drugs that are not manufactured in Indonesia locally (UNCTAD, 2011a). A final case that has received much attention is that of India, wherein the pre-TRIPS IPRs regime did not recognize product patents for pharmaceuticals and gave process patent protection only for a period of seven years.

#### ***III.2.4 Preventing the Importation of Lax Patenting Criteria from Abroad***

There is a need to stipulate a rigorous inventive step as part of patenting criteria in national patent regimes in developing and least developed countries. Developing such new criteria to evaluate patentability that exploit available TRIPS flexibilities to their fullest extent is far more difficult when compared to simply adopting prevalent intellectual property solutions from the global west.<sup>64</sup> Recent analysis and evidence suggest that patent offices in developing countries are historically conditioned to take on board time-tested IP interpretations when deciding under uncertainty.<sup>65</sup> As a result, it is likely that dominant trends on a lax inventive step will permeate patenting standards in developing countries as well, unless clear policy action is taken to define rigorous inventive step within national patent laws.

A distinction needs to be made between the patenting criteria and the lack of technical capacity in developing countries to implement these criteria. It is true that very few developing and least developed countries have the ability to substantially evaluate patent claims and therefore rely on the decisions of other jurisdictions to decide whether to grant patents or not. This simply means that patent grants are not made on an informed basis, simply because of the lack of technical capacity of the countries to do so. However, when the standards of patentability are

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<sup>64</sup> See Drahos (2007) who notes that "...[d]eveloping country patent offices 'have been integrated into a system of international patent administration in which the grant of low-quality patents by major patent offices is a daily occurrence.' See also Correa (2008).

<sup>65</sup> Drahos (2010). Forero-Pinada (2006, p. 208) notes that "the trend...has extended from developed to developing countries, affective even pharmaceuticals and medical devices, where for several decades, developing countries had imposed restrictions on patenting or simply refused to allow it."

clearly provided for within national patent regimes, local firms can rely on pre-grant or post grant oppositions (if allowed in national laws) or litigation as recourse to get patents on incremental innovations revoked.<sup>66</sup>

#### **IV. CONCLUDING REMARKS**

This paper has analysed two important issues in promoting local pharmaceutical capacity in developing and least developed countries within the TRIPS framework. The first issue relates to whether a lax standard of inventive step would promote the growth of a local pharmaceutical sector in developing countries. Using both theoretical and empirical arguments, the paper argues that both the nature of pharmaceutical learning and innovation and the interest of public health are best served in a framework where more rigorous standards of inventive step are used to grant patents. The analysis suggests that local firms in developing and least developed countries are better supported in a framework where patent protection for incremental innovations is not allowed, making it easier for them to produce using existing technological base of the sector, while seeking to expand their knowledge base. The paper also shows that although some countries have used variations such as utility models to promote inventive activity in other sectors in economic history, these countries only provided a low level of novelty within their domestic regimes to incentivize the local firms, and not a low inventive step. A lax (low level of) inventive step, the paper argues, has several detrimental impacts for developing countries. First, a low inventive step is prone to abuses, leading to unnecessary extension of patent monopolies through products embodying minor changes, thereby also affecting access to medicines. Second, it can lead to overly fragmented technological domains and difficulties in accessing knowledge, which is detrimental to building technological capacity for production and innovation in the pharmaceutical sector in developing countries.

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<sup>66</sup> Litigating patent claims is clearly a costly process across the world, and hence, the practice of simply granting patents without considerable evaluation of its social and public health impacts, and relying on the litigation process to “clean up” the market is not really in the interest of local firms and public health.

A second issue that this paper has dealt with relates to the relationship between a rigorous inventive step and compulsory licensing. Using several recent examples of drugs that have been compulsory licensed in developing countries, the analysis concludes that countries could well avoid spending political capital on efforts to compulsory license drugs if they used more rigorous definitions of inventive step to grant patents on drugs. Since drugs subject to compulsory licenses/government use are usually imported, a rigorous inventive step also implies greater potential for local firms to engage in generic production and greater health security in developing countries in the long run.

Reviewing all the major country experiences on compulsory licenses, the paper arrives at the following conclusions:











1. While compulsory licenses have resulted in substantial price reductions, they have been largely used by the larger and more powerful developing countries which have effective mechanisms for compulsory licenses/government use, and the adequate political will to use the mechanism. It is a combination of these two factors that has helped such countries to negotiate reasonable prices and access conditions to patented products.
2. This could have two important positive consequences to developing countries. First, some of the CLs that were issued by the bigger countries could have been avoided if they had specified a rigorous standard of inventive step within their national regimes. The analysis in section 3 of the paper provides a number of examples of drugs that have been the subject of efforts for CL, which are incremental innovations. Stipulating a rigorous inventive step would help avoid the unnecessary use of political capital in issuing CLs as an aftermath. This is all the more true in the case of smaller developing countries and least developed countries that have much less ability to withstand the political pressure and scrutiny involved in granting CLs. Second, as opposed to granting licenses that lead to the importation of the drug, specifying a rigorous standard of inventive step can foster local pharmaceutical production in developing countries through the non-










issuance of patents on incremental pharmaceutical innovations.











3. In the absence of national regimes that provide a rigorous inventive step, there is a realistic possibility that lax patenting criteria will permeate patent offices and courts in developing countries as a default legal position. In order to avoid this, more rigorous patenting criteria need to be defined within national regimes.
4. Despite the definition of a rigorous inventive step, national regimes may lack the technical capacity to implement these standards. This calls for greater capacity building of national patent offices and legal officials working in courts and patent tribunals.

The paper has also brought out some other results on compulsory licensing. An important issue relates to the policy position of countries in choosing CLs as an option. The available evidence seems to indicate that countries that have some local capacity (in terms of either private or government owned firms) or those that are obliged to provide cheaper drugs for their populations are most inclined to use the mechanism. In the case of the former, the compulsory license was used to as a political instrument to signal the importance the country gives to greater access to medicines of importance to public health. Coincidentally, these are countries that generally have supportive policy frameworks to promote local production of medicines in the interest of public health. In these cases, there are limitations in investment of the foreign firms, their terms of engagement, and pricing, such as Indonesia and to a certain extent Brazil. Therefore, impact on patent holders in terms of FDI, or other marketing options are minimal. The other countries that seek to use compulsory licenses without this strategic perspective seem to have limited use of the instrument. This issue needs to be analysed in greater detail.











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## **CHAPTER 8**

### **STRENGTHENING PATENT STANDARDS: AN ALTERNATIVE ROUTE TO COMPULSORY LICENSING FOR LOW AND MIDDLE INCOME COUNTRIES**

Priti Radhakrishnan and Tahir Amin

#### **I. INTRODUCTION**

There is growing evidence about the proliferation of patents over minor variants of existing products both in developed and developing countries. Patents on incremental developments can deter competition and, in some cases, genuine follow-on innovation. This trend raises concerns about the role of the patent system in promoting social welfare and legitimate inventive activity.

The observed trend has special implications in the case of pharmaceuticals. While the number of newly-developed chemical entities has dramatically fallen during the last 10 years, the number of patents over simple changes in chemistry/formulation of existing pharmaceutical products (e.g. polymorphs, combinations, dosage forms, isomers) has continuously increased. The strategic use of incremental patenting to exclude or delay generic competition may block access to affordable drugs and constitutes an important obstacle for the realization of the right to health. As a result of such delays or extended monopolies, in order to meet public health needs, governments are forced to resort to price negotiations or issuing compulsory licenses/government use.

In view of these implications, many academics and NGOs have advocated the adoption of more stringent criteria to assess patentability, so as to prevent the grant of patents that do not make a substantive technical contribution to the state of the art. Some governments, for example India, have implemented legislation or policies to this effect.

On the other hand, it has been argued that a patent policy that broadly allows for the protection of minor innovations may benefit local industries in developing countries. While fundamental innovations are out of their reach, they might strengthen their competitive capacity by developing and patenting minor innovations.

Recent experiences (for example, in Thailand) show that the application of low standards of patentability has led in some cases to the grant of patents that later may need to be subjected to a compulsory license/government use. Although government use and compulsory licenses are legitimate under international law, the application of these provisions has faced considerable resistance from developed country governments and retaliations from the pharmaceutical industry.

Based on this, the question of whether with the application of well-defined patentability standards, governments could avoid spending the political capital necessary to grant and sustain compulsory licenses/government use is explored. Under such a theory, if patent applications were scrutinized with rigorous patentability standards by patent offices, there would be no patent grant and, hence, no need to have recourse to these measures. This chapter examines case studies of compulsory licenses requested or issued in developing countries and the political costs involved. The report then assesses the patent quality of a selection of the patents for which licenses have been requested and whether rigorous patentability criteria would have removed the need in those cases for governments to traverse the compulsory licensing route.

## **II. METHODOLOGY**

The initial step was to identify where compulsory licenses had been requested, and granted or refused. The type of compulsory license that was requested and/or granted was then identified, given that there are different kinds. Compulsory licenses for public health purposes typically fall under one of the following types:

- a) a compulsory license issued three years after the grant of a patent as a result of the invention not being reasonably available to the public or is being used anti-competitively;

- b) a compulsory license issued in the case of a national emergency, extreme urgency or for public non-commercial use;
- c) a compulsory license issued for import/export purposes where the importing country has insufficient or no manufacturing capacity;
- d) government use of the patented invention for government needs.

In each of these cases, the patent holder is compensated.

After review of the type of compulsory license requests made, the political impact and costs to countries for pursuing such policy choices were considered. Since pressure from patent holders and governments largely occur outside of the purview of public channels, the assessment provided here largely relied on secondary sources, that is, NGOs and the media, reports. Where primary information was publicly available, such as the United States Trade Representative (USTR) Special 301 reports or submissions by PhRMA to the USTR, it was referenced.

The final step was to take a sample of the patents for which price negotiations or compulsory licenses had been requested and assess whether such strategies would have been necessary under more stringent patentability criteria (including the early introduction or retrospective protection for pharmaceutical product patents). Ideally, the methodology would have entailed access to all the relevant national patent documents and local patentability laws related to the relevant compulsory license request. The exercise of gathering or accessing these materials was too resource intensive or not possible due to patent documents and local legislation being unavailable. Therefore the patentability assessments were made by referencing cases where such patents have been refused in other countries, equivalent US or European patents, information gathered as a result of work on patent oppositions in relation to some of the patents discussed and/or using the standards set out in Carlos Correa's work 'Guidelines for the Examination of Pharmaceutical Patents'.<sup>1</sup>

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<sup>1</sup> Correa, C, *Guidelines for the Examination of Pharmaceutical Patents: Developing a Public Health Perspective* (World Health Organization, International Centre for



### III. CASE STUDIES OF GRANTED COMPULSORY LICENSES

#### III.1 High Profile Examples of Compulsory Licenses

This section looks at compulsory licenses that have attracted significant international scrutiny. Countries that have incurred significant political pressure, for example, Brazil and Thailand possess manufacturing capacity and pose a threat to the multinational pharmaceutical industry. Some commentators have noted the industry's position that industrial policy, or the growth of domestic manufacturing capacity, is driving low-and middle-income countries to issue compulsory licenses.<sup>2</sup> These issues form the complex interplay between politics, compulsory licensing, price reductions and access to medicines.

##### Brazil

Brazil introduced pharmaceutical product patents in 1997, around eight years prior to that permitted under the transitional provisions under the Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS).<sup>3</sup> Not only did Brazil implement its product patent regime earlier than required, it also extended the law to allow patent holders to apply for protection of inventions patented in other countries prior to TRIPS. This allowance of retrospective protection of patents is known as the pipeline provision. In 2009 it was estimated that of the 1,182 patents filed under the pipeline provision, approximately 700 had been granted.

Some of these patents include key medicines such as abacavir, efavirenz, imatinib (Glivec), ritonavir and lopinavir.<sup>4</sup>

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Trade and Sustainable Development, United Nations Conference on Trade and Development and the United Nations Development Programme, January 2007).

<sup>2</sup> Deere, C, *The Implementation Game: The TRIPS Agreement and the Global Politics of Intellectual Property Reform in Developing Countries*. (2009, at p 231).

<sup>3</sup> Law No. 9.279/96 (Industrial Property Act). The law recognized what have been termed 'pipeline patents': it allowed the filing of patent applications during a one-year-period (May 1996 to 1997) for inventions that had lost novelty, provided that they had not been commercialized yet in any country and that there were no serious preparations for their exploitation in Brazil.

<sup>4</sup> Information provided by Associacao Brasileira Interdisciplinar de AIDS (ABIA) at the meeting '*Examination of Pharmaceutical Patents: Arguing from Public Health Perspective*', Rio de Janeiro, 18 November 2008.

The Constitution approved in 1988, allowed the introduction of a universal health care programme. As the number of HIV/AIDS cases increased, the cost of ensuring free access to antiretrovirals (ARVs) began to stretch the budget of Brazil's National AIDS Programme.

As a result, between 2001 and 2003, Brazil negotiated discounts from originator companies on the HIV drugs nelfinavir and efavirenz, in part due to its announcements to issue compulsory licenses.<sup>5</sup> However, by 2003, three patented drugs – nelfinavir, efavirenz and lopinavir/ritonavir – were still making up 63 per cent of the national HIV treatment budget.<sup>6</sup> It came as no surprise when, in 2005, Brazil requested that Abbott Laboratories offer a new, discounted price on lopinavir/ritonavir. It did so after announcing the patent of lopinavir/ritonavir in the public interest and suitable for compulsory licensing.<sup>7</sup> Abbott did reduce the price by 46 per cent, but only after extracting concessions from the Brazilian government, including a retreat on compulsory licensing of the drug, and a freeze on any price negotiations for 6 years.<sup>8</sup>

The political costs of this settlement are well-documented. The head of the AIDS programme is on record stating that Brazilian government officials were subjected to lobbying from the US, including Congress and the White House, with threats of retaliation (Deere, 2009, p.230). Civil society took both Abbott and the Brazilian government to court, but judges have halted the action, citing trade retaliation from the United States, as well as the inability of Brazilian manufacturers to produce the drug domestically.<sup>9</sup>

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<sup>5</sup> Deere. C, *The Implementation Game*, (2009, pp. 230-231). See also Love. J, *Recent Examples of the Use of Compulsory Licenses on Patents* (KEI Research Note, 2007, p 15).

<sup>6</sup> Deere. C, *The Implementation Game*, (2009, pp. 230-231). See also Love. J, *Recent Examples of the Use of Compulsory Licenses on Patents* (KEI Research Note, 2007, p 15).

<sup>7</sup> Love. J, *Recent Examples of the Use of Compulsory Licenses on Patents* (KEI Research Note, 2007 at p 15).

<sup>8</sup> Deere at pp. 230-231, See also Ford et al, "Sustaining access to antiretroviral therapy in the less-developed world: lessons from Brazil and Thailand", (2007 at p S26), and Love at p 15.

<sup>9</sup> Ford et al, "Sustaining access to antiretroviral therapy in the less-developed world: lessons from Brazil and Thailand", (2007, p. S26). See also Renata Reis, Marcela

Eventually Brazil was successful in its efforts to issue a compulsory license for the HIV drug efavirenz in 2007. The government began importing the drug from India, and faced considerable pressure from Merck, the patent holder, in doing so (Ford et al, 2007, P. S23).

### Canada-Rwanda

In 2007, using the flexibilities provided under Paragraph 6 of the Doha Declaration (the World Trade Organization August 30 Decision) which allows for countries with insufficient or no manufacturing capacity to issue compulsory licenses, Rwanda notified the TRIPS Council of its issuance of a license on the HIV drug combination lamivudine, zidovudine and nevirapine.<sup>10</sup> Shortly thereafter, Canada issued a compulsory license for nine patents related to Triavir, the Canadian name for this drug combination.<sup>11</sup> The Canadian license was designated only for manufacture and export to Rwanda.<sup>12</sup>

This set of compulsory licenses was the first to be issued under the August 30 Decision, wherein the World Trade Organization expanded the use of compulsory licenses from primarily domestic purposes to allow for export.<sup>13</sup> Canada was one of several countries—including Norway, China, India and the European Union, among others—that adopted legislation to implement the August 30 Decision.<sup>14</sup> Despite

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Foçaça Vieira and Gabriela Chaves. “Access to medicines and intellectual property in Brazil: a civil society experience”, in *Intellectual Property Rights and Access to ARV Medicines: Civil Society Resistance in the Global South*. Rio de Janeiro, ABIA, 2009.

<sup>10</sup> Deere, 2009, p. 230. See also, Hestermeyer, Holger P., “Canadian-made drugs for Rwanda: the first application of the WTO waiver on patents and medicines” *American Society of International Law*, 10 December, 2007. Available from <http://www.asil.org/insights071210.cfm>.

<sup>11</sup> Deere, 2009, p. 230. See also Hestermeyer, Holger P., “Canadian-made drugs for Rwanda: the first application of the WTO waiver on patents and medicines”, *American Society of International Law*, 10 December, 2007. Available from <http://www.asil.org/insights071210.cfm>.

<sup>12</sup> Deere, 2009, p. 230. See also, Hestermeyer, Holger P., “Canadian-made drugs for Rwanda: the first application of the WTO waiver on patents and medicines” *American Society of International Law*, 10 December, 2007. Available from <http://www.asil.org/insights071210.cfm>.

<sup>13</sup> Neither expeditious, nor a solution: the WTO August 30th Decision is unworkable (Médecins Sans Frontières, 2006).

<sup>14</sup> *Ibid.*

this step, and several efforts by Médecins Sans Frontières and Apotex, a generic company, five years passed before export of Triavir was initiated.<sup>15</sup>

The August 30 Decision is widely criticized as practically unfeasible. Compulsory licensing for export is difficult, whether for political pressures or its burdensome implementation. The TRIPS Council reviews the August 30 Decision every year to determine how it can be strengthened. In the absence of a workable compulsory license mechanism for export, stronger patentability criteria could help lower barriers to access. In this case, however, it would be insufficient for the low-income country to act alone. Rather, the developed country would also need stronger patentability criteria. Countries adopting stricter legislation or implementation of patentability criteria may remove onerous obstacles to access to medicines in the long term.

### Thailand

The Thai experience with compulsory licensing has spanned a decade. In 1999, Thai civil society requested a license on the tablet form of the HIV drug didanosine.<sup>16</sup> This move was spurred in part by the Thai experience with fluconazole, a treatment for cryptococcal meningitis. The year before, the Thai Government initiated domestic production of fluconazole, and the price of the drug dropped by 97 per cent.<sup>17</sup> Realising the cost savings of generic versions, irrespective of the fact that fluconazole was not a case of a patented drug, the impact prompted the request for a compulsory license on didanosine.

The response from the U.S Government was swift, and cautioned against the use of compulsory licenses. Despite strong advocacy from Thai civil society, the Thai Government did not issue a compulsory license on the didanosine tablet. Instead they authorized

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<sup>15</sup> An Unsolved Problem: The August 30 Decision. Available from <http://www.msface.org/main/access-patents/introduction-to-access-and-patents/trips/an-unsolved-problem-the-august-30th-decision/>.

<sup>16</sup> t'Hoen, E, *The Global Politics of Pharmaceutical Monopoly Power*, (2009, pp. 23-25).

<sup>17</sup> Ibid.

generic production of an older powdered form of the drug, which would not infringe the tablet patent held by Bristol Myers Squibb.<sup>18</sup>

Several years later, in 2006, the Thai Minister of Public Health determined that a compulsory license was required for efavirenz, an HIV drug offered by Merck at high prices, with frequent stockouts (Ford et al, 2007). Merck responded with a two-pronged strategy, dropping its own prices, and lobbying the US Government to pressure the Thai Government. Despite the intense pressure, the Thai Government issued the license and began importing generic efavirenz.

Following this, the Thai Government issued compulsory licenses on clopidogrel, popularly known as Plavix for the treatment of heart disease, and for the HIV drug lopinavir/ritonavir.<sup>19</sup> The political costs for the license on the HIV drug were significant – Abbott Laboratories, the originator company behind the drug, engaged in a dramatic lobbying campaign to block the license, including withdrawing all their drug products from the Thai market. Abbott Laboratories also influenced the US Trade Representative to pressure the Thai Government.<sup>20</sup> International stakeholders, including former President Bill Clinton and key members of Congress, acted swiftly to support the Thai Government, and generic affordable versions of these drugs continued to be available in Thailand. The Thai Government is an excellent case study of the political cost to developing countries when they lawfully utilize TRIPS flexibilities.

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<sup>18</sup> Ibid.

<sup>19</sup> *Facts and Evidences on the 10 Burning Issues Related to the Government Use of Patents on Three Patented Essential Drugs in Thailand*, by the Ministry of Public Health and National Health Security Office, February 2007.

<sup>20</sup> James Love, “Merck, USTR ask Thailand to reconsider compulsory license on AIDS drug”, *Huffington Post*, 18 December 2006. Available from [http://www.huffingtonpost.com/james-love/merck-ustr-ask-thailand-t\\_b\\_36643.html](http://www.huffingtonpost.com/james-love/merck-ustr-ask-thailand-t_b_36643.html).

### **III.2 Examples of Compulsory Licenses Attracting a Mid-range Level of Political Consideration**

#### Ecuador

In 2010, Ecuador issued a compulsory license on the HIV drug ritonavir, owned by Abbott Laboratories. The license was granted to Eskegroup SA, a distributor of Cipla. Eskegroup agreed to pay Abbott a royalty based on the ‘tiered method’ adopted by the UNDP and WHO, which constitutes 4 per cent of the high income country price, adjusted by factors related to income and disease burden in country.<sup>21</sup> According to the country’s intellectual property office, increased competition facilitated significant cost savings.<sup>22</sup> These potential cost savings are particularly significant because lopinavir, the protease inhibitor often co-formulated with ritonavir, is reportedly not patented in Ecuador.<sup>23</sup>

Ecuador’s recent issuance of a compulsory license met with little or no backlash from the pharmaceutical industry or the U.S. Government. Potential reasons for the lack of outcry include Ecuador’s status as a low-middle income country, and the precedent set during the Thai experience, when the international public decried the USTR and Abbott treatment of the Thai Government. In relation to the Ecuador license, Abbott merely released a statement expressing ‘disappointment’.<sup>24</sup>

Ecuador’s HIV treatment programme was expected to expand in part due to savings created by this license.<sup>25</sup> The treatment programme was meeting the needs of 42 per cent of Ecuadorians requiring treatment at the time the compulsory license was granted.<sup>26</sup>

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<sup>21</sup> Saez, C, “Ecuador grants first compulsory license, for HIV/AIDS Drug”, 22 April 2010. Available from <http://www.ip-watch.org/weblog/2010/04/22/ecuador-grants-first-compulsory-licence-for-hiv-aids-drug/>.

<sup>22</sup> Ibid.

<sup>23</sup> Ibid.

<sup>24</sup> Ibid.

<sup>25</sup> “Praise for Ecuador’s grant of compulsory license for AIDS drug”, SUNS, 30 April 2010. Available from <http://www.twinside.org.sg/title2/health.info/2010/health20100502.htm>.

<sup>26</sup> Ibid.

### Taiwan

Taiwan was the first country to respond to the avian flu crisis in 2005 with a compulsory license for oseltamivir, commercially known as Tamiflu.<sup>27</sup> The Taiwanese Government issued the compulsory license to permit domestic production of oseltamivir.<sup>28</sup> The license, granted to the Taiwanese Department of Health (DoH), allowed the DoH to produce oseltamivir on its own, or source from a local producer.<sup>29</sup> Due to political considerations however, the government through the Intellectual Property Office (TIPO) restricted the license on four grounds.<sup>30</sup> First, the DoH had to exhaust its existing supply of the drug from Roche. Second, the license was confined to use within Taiwan, and expired by the end of 2007. Third, the DoH had to pay a reasonable royalty to Roche. Lastly, the license was retractable if the DoH and Roche could agree on the terms of a voluntary license. Roche proclaimed that its commitment to supply Taiwan with a substantial volume of oseltamivir would nullify the need for domestic production, in the absence of a pandemic. Although it was reported the DoH would commence production irrespective of Roche's commitment, it is not known whether this was acted upon.

The same year, in 2005, Taiwan was reinstated on the USTR's Special 301 Watch List, after being downgraded from the Priority Watch List in 2004.<sup>31</sup> Despite being reinstated on the Special 301 Watch List, overall there appeared to be a lack of political backlash around the oseltamivir license. This could be possibly attributed to Taiwan agreeing in 2005 to introduce a data exclusivity provision protecting test data on pharmaceuticals.<sup>32</sup>

### Indonesia

In 2004, Indonesia issued compulsory licenses for government use on

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<sup>27</sup> Taiwan Issues Compulsory License for Tamiflu (ICTSD, 30 November 2005). Available from <http://ictsd.org/i/ip/39838/>.

<sup>28</sup> See Taiwan employs compulsory licensing for Tamiflu, by Kathrin Hille, 25 November 2005. Available from <http://news.ft.com/cms/s/cebeb882-5dcb-11da-be9c-0000779e2340.html>.

<sup>29</sup> *Ibid.*

<sup>30</sup> *Ibid.*

<sup>31</sup> The downgrade occurred at the end of 2004. See USTR Special 301 Reports from 2005 and 2006.

<sup>32</sup> USTR Special 301 Report 2005, pp.47-48.

two HIV drugs. A Presidential Decree stated that lamivudine and nevirapine were both necessary to urgently respond to the HIV epidemic, and authorized the Minister of Health to appoint a public factory to provide the generic version of the drugs. Under the terms of the license, Indonesia committed to paying a 5 per cent royalty to the patent holders. The compulsory licenses were to run through the patent terms, expiring in 2011 and 2012, respectively. This action by the Indonesian government drew very little international scrutiny and was not directly addressed by the USTR, despite Indonesia's inclusion on the Priority Watch List.<sup>33</sup>

Subsequently in 2005, Indonesian officials reported that the drugs were available in government-run hospitals and that the cost of treatment had been substantially lowered.<sup>34</sup> Reports also indicate that the production of the ARVs was done by PT Kimia Farma (Love, 2007, p. 12). In 2007, independent groups initiated efforts to persuade the government to issue compulsory licenses for second-line HIV drugs.<sup>35</sup> In the same year, the government reportedly issued a compulsory license on the patents for the HIV drug efavirenz (Love, 2007, p. 12).

### Malaysia

In 2004, Malaysia approved compulsory licenses for government use on three HIV drugs, didanosine, zidovudine and a combination drug, lamivudine/zidovudine (Deere, 2009, p. 230). The two-year licenses were issued by the Minister of Domestic Trade and Consumer Affairs, and a royalty rate of four per cent of the value of actual generic imports was proposed by the Ministry of Health.

The license escaped international scrutiny in public fora (Deere, 2009, p. 231), but lobbying efforts by the U.S behind the scenes indicated that the Malaysian Ministry came under tremendous pressure.

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<sup>33</sup> Deere, 2009, p. 230. See also USTR Report 2005.

<sup>34</sup> Shashikant. S, "More countries use compulsory license, but new problems emerge", 19 May 2005. Available from <http://www.twinside.org.sg/title2/health.info/twinfohealth004.htm>.

<sup>35</sup> "Indonesia mulls compulsory licenses on three more HIV/AIDS drugs" *Intellectual Property Watch*, 26 November 2007. Available at <http://www.ip-watch.org/weblog/2007/11/26/indonesia-mulls-compulsory-licences-on-three-more-hiv-aids-drugs/>.



It is understood GlaxoSmithKline filed a lawsuit after the government use license was issued, but neglected to activate the suit.<sup>36</sup> The Ministry also reported that the patent holders were not accepting the reasonable remuneration.<sup>37</sup> Later in 2004, at an Asean workshop on compulsory licensing in Malaysia, the Minister of Health stated that it would be very difficult for Malaysia to repeat the process of compulsory licensing again.<sup>38</sup>

### Mozambique

The Ministry of Commerce and Industry issued a compulsory license on HIV drugs in 2004.<sup>39</sup> Citing the ravaging toll of the epidemic in the country, the government authorized local production of a fixed-dose combination of lamivudine, stavudine and nevirapine.<sup>40</sup> The license notes the absence of a branded version of this fixed-dose combination in the country.<sup>41</sup> The license authorized Pharco Mocambique Lda to locally produce this combination drug with royalties capped at 2 per cent of total annual turnover.<sup>42</sup> The license was issued until “conditions of national emergency and extreme urgency created by the HIV/AIDS pandemic will come to an end”.<sup>43</sup>

It appears very little attention was paid to Mozambique’s issuing of a compulsory license. This could be due to the fact that lamivudine, stavudine and nevirapine are understood to have not been patented in Mozambique.<sup>44</sup>

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<sup>36</sup> Ling. C.Y. *See Malaysia’s Experience in Increasing Access to Antiretroviral Drugs: Exercise the “Government Use” Option*, Third World Network. Available from <http://www.twinside.org.sg/title2/IPR/pdf/ipr09.pdf>.

<sup>37</sup> Ibid.

<sup>38</sup> As told to author, at the Asean Workshop on Compulsory Licensing to Increase Access to Antiretrovirals, Kuala Lumpur, Malaysia in 2004.

<sup>39</sup> Mozambique Compulsory License no. 01/MIC/04. Both Portuguese and translated versions available from <http://www.cptech.org/ip/health/c/mozambique/>.

<sup>40</sup> Ibid.

<sup>41</sup> Ibid.

<sup>42</sup> Ibid.

<sup>43</sup> Ibid.

<sup>44</sup> Attaran. A and Gillespie-White. Lee, “Do patents for antiretroviral drugs constrain access to AIDS treatment in Africa?” *Journal of American Medical Association*, vol. 286, No. 15 (17 October 2001).

## Zambia

Pointing to the extreme prevalence of the HIV epidemic in country, the Minister of Domestic Trade and Consumer Affairs issued a compulsory license for a fixed-dose combination HIV drug in 2004. The license authorized a local company, Pharco Ltd, to produce a three-in-one pill of lamivudine, stavudine and nevirapine, with a maximum royalty rate of 2.5 per cent. The license made special mention of the lack of cooperation between the three originators to develop this combination, and the absence of the combination drug in Zambia. The expiration of the license was set as the end date of the “national emergency and extreme urgency created by HIV pandemic” in Zambia, or at the end of the emergency period set out by law.

Again, the issuing of the compulsory license appeared to fly under the radar of the media and any public government or company reaction. This is noteworthy since it is believed lamivudine and nevirapine were protected by patents in Zambia.<sup>45</sup>

### **III.3 Low-profile Examples of Compulsory Licenses**

#### Broad based Licenses

Several African countries have opted for a broad compulsory license to import affordable generic HIV drugs. From 2002-2005, Eritrea<sup>46</sup>, Ghana<sup>47</sup>, Guinea<sup>48</sup>, Swaziland (Love, 2007) and Zimbabwe<sup>49</sup> all issued

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<sup>45</sup> Ibid.

<sup>46</sup> For original license, see <http://www.cptech.org/ip/health/cl/recent-examples.html#Eritrea>.

<sup>47</sup> For original license, see <http://www.cptech.org/ip/health/cl/Ghana.png>.

<sup>48</sup> Love, J, Recent Examples of the Use of Compulsory Licenses on Patents (KEI Research Note, 2007), and also Duncan Bucknell, “Worldwide: the global IP scorecard for pharma & biotech compulsory licenses”. (23 October 2007). Available from <http://www.mondaq.com/australia/article.asp?articleid=53442>.

<sup>49</sup> For the original license, see <http://www.cptech.org/ip/health/c/zimbabwe/zim05242002.html>. Zimbabwe extended emergency in 2003 through 2008. Working with India, Zimbabwe started local production through Varichem Pharmaceuticals (Pvt) Ltd. The Médecins Sans Frontières press release on the Zimbabwe compulsory license noted specific drugs that were patented or had patents pending, including GlaxoSmithKline's zidovudine (AZT), lamivudine (3TC), abacavir (ABC), AZT/3TC, and AZT/3TC/ABC, and Boehringer-Ingelheim's nevirapine. For the full press release, see

letters to override patents where necessary to meet the domestic needs of their HIV populations.

<b>Country</b>	<b>Issuing Body</b>	<b>Issued To</b>	<b>Relevant Language</b>
Eritrea	Ministry of Health	IDA procurement agency	After careful review of WTO rules, declares emergency to import generics only for non-commercial purposes, speed up supply.
Guinea	Not Available	Not Available	Not Available
Swaziland	Ministry of Health	Not Available	Noted emergency, and permitted procurement of HIV drugs in the best cost effective way possible, despite patents, until it was no longer essential to address the public health crisis in this way.
Zimbabwe	Minister of Law, Justice and Parliamentary Affairs	General Issuance	Addressed a state of emergency for 6 months. Allowed for manufacture, use or import of patented HIV drugs under section 34 of law, and expressly permitted importation of generic drugs.

These compulsory licenses differ from those of other countries because they do not explicitly set out the drugs to be licensed. Rather, these countries chose to permit all HIV drugs to be available generically to meet their domestic needs. Based on available licenses, it appears that

these countries used statutory provisions for emergency compulsory licensing and/or government use.

These licenses appear to have garnered minimal attention in the press, and are omitted from industry press statements of that time period (Deere, 2009, p. 231). Notably, the USTR does not make mention of these licenses in the Special 301 Watch List.<sup>50</sup>

#### **IV. CASE STUDIES OF UNSUCCESSFUL/PENDING REQUESTS FOR COMPULSORY LICENSING**

##### South Korea

In 2002, various concerned actors filed a request for a compulsory license on imatinib mesylate, also known as Glivec. The request was denied by the Korean Intellectual Property Office in 2003.<sup>51</sup> The decision was based on two factors. First, a license was not necessary because leukemia was not an infectious disease, or poised to cause an extremely dangerous situation in Korea. These facts, balanced against the purpose of the patent system, did not necessitate a license. Second, CML patients at this time were purportedly covered under health insurance, bearing 10 per cent of the cost of medicines. According to the decision, this was not considered to be sufficient to warrant a license in the public interest.<sup>52</sup>

In 2005, the Food and Drug Administration in Korea contemplated issuing a compulsory license on oseltamivir.<sup>53</sup> Ultimately, Roche issued a voluntary license.<sup>54</sup>

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<sup>50</sup> Referring to Special 301 Report Watch List by the United States Trade Representative from 2002-2005.

<sup>51</sup> Decision on the Request for Adjudication for the Grant of a Non-Exclusive License. Available from [http://glivec.jinbo.net/Decision\\_CL\\_Glivec.htm](http://glivec.jinbo.net/Decision_CL_Glivec.htm).

<sup>52</sup> *Ibid.*

<sup>53</sup> Cheong-won. W, "Health Regulator Seeks to Produce Bird Flu Drug", *Korea Times*, October 2005. Available from <http://times.hankooki.com/lpage/nation/200510/kt2005103118142611960.htm>.

<sup>54</sup> Hyun-joo. J, "Korea Seeks Tamiflu Joint Production", *Korea Herald*, 6 April 2010. Available from <http://www.koreaherald.com/national/Detail.jsp?newsMLId=20051103000038>.

In 2009, the Korean Ministry of Health was in discussion with Roche to address the pricing of Fuzeon an HIV drug. Korean patient groups and NGOs filed requests for a compulsory license, citing that the price of the drug was out of reach. The Korean Intellectual Property Office (KIPO) rejected the request for a compulsory license on Fuzeon. It is reported that the request was rejected by KIPO on the grounds that based on the totality of the facts, a compulsory license was not “especially necessary for the public interests” in this case.<sup>55</sup> Moreover, KIPO found that granting a compulsory license would likely damage the fundamental nature of patent rights, particularly if the only reason for lack of access was due to drug pricing negotiation issues.

#### Lopinavir/Ritonavir: Colombia

In 2009 the Colombian Government rejected a request for compulsory licensing the HIV drug lopinavir/ritonavir.<sup>56</sup> As a result of the request, the government set maximum prices for the drug, bringing the price down by 54-68 per cent. According to government statements, the cost savings from these price reductions are over \$10 million per year.

#### South Africa

In 2001, Cipla requested the South African Government to issue compulsory licenses on several drugs, including nevirapine, lamivudine, zidovudine, stavudine, didanosine, efavirenz, indinavir, abacavir, and combinations of these drugs.<sup>57</sup> The request was denied (Deere, 2009, p. 231).

#### Dominican Republic

The Dominican Republic has consistently drawn the ire of the USTR and the multinational pharmaceutical industry, as indicated by its placement on the USTR’s Special 301 Watch List.<sup>58</sup> One reason for this

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<sup>55</sup> Kim. Y and Kim. J, *Rejection of Compulsory License for AIDS Drug Patents Becomes Final*, World Intellectual Property Report, (February 2010).

<sup>56</sup> Colombian Government Refuses Request to Issue Compulsory License on Expensive HIV/AIDS Drug, June 3 2009. Available from [http://www.essentialaction.org/access/?/archives/183-Colombian-Government-Refuses-Request-to-Issue-Compulsory-License-on-Expensive-HIV/AIDS-Drug\\_html&paged=5](http://www.essentialaction.org/access/?/archives/183-Colombian-Government-Refuses-Request-to-Issue-Compulsory-License-on-Expensive-HIV/AIDS-Drug_html&paged=5).

<sup>57</sup> Cipla’s 7 March 2001 Compulsory Licensing Request, available from <http://www.cptech.org/ip/health/sa/ciplanetsh03072001.html>.

<sup>58</sup> See <http://lists.essential.org/pipermail/pharm-policy/2000->

was the incorporation of several TRIPS flexibilities into the industrial property law in 2000.

Requests for compulsory licenses have not been fruitful, such as on the drug clopidogrel, popularly known as ‘Plavix’ as branded by Bristol Myers Squibb and Sanofi Aventis, a French company (Love, 2007, p. 14). The French embassy is reported to have written to the Secretary of State of the D.R. to voice opposition to the compulsory license request (Love, 2007, p. 14).

Other strategies have been more successful. When Rowe, a domestic pharmaceutical manufacturer introduced a generic version of the HIV drug indinavir, Merck significantly reduced its prices by approximately 85 per cent on indinavir and efavirenz, another HIV drug.<sup>59</sup>

#### Ecuador

Past attempts at compulsory licensing in Ecuador have met with rejections from the government, most notably in 2003. Acromax, a domestic producer, applied on more than one occasion to produce a lamivudine/zidovudine combination, marketed as Combivir.<sup>60</sup> Despite the rejection for the compulsory license, Glaxo reduced its prices on all HIV drugs for Ecuador.<sup>61</sup>

## **V. STRICT PATENTABILITY CRITERIA VS. COMPULSORY LICENSING**

This section reviews a sample of the patents relating to the compulsory licenses (including negotiations for price reduction) that have been requested and/or granted above and makes a broad assessment on

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September/000348.html, See also

<http://www.cptech.org/ip/health/c/dr/healthgap08092001.html>.

<sup>59</sup> Correspondence from Ho Chi Vega to James Love, available from <http://lists.essential.org/pipermail/pharm-policy/2001-August/001425.html>.

<sup>60</sup> Ibid.

<sup>61</sup> Ibid.

whether they would have been patentable under more stringent patentability criteria.

### **V.1 Brazil's Price Negotiations on Ritonavir/Lopinavir**

The priority filing date for the patent covering the base compound of ritonavir pre-dates Brazil's introduction of pharmaceutical product patent protection. However, as Brazil elected to introduce retrospective pipeline protection for inventions filed prior to TRIPS, ritonavir could be under patent, as it is the case of patents for lopinavir/ritonavir.

Had Brazil not introduced pipeline protection the key blocking patent on lopinavir would not have been granted in Brazil. Abbott's subsequent patents following the base compound patent for lopinavir relate to incremental type patents including new formulations, such as the solid dispersion form (also known as the heat-stable form).

Rigorous patentability criteria such as India's 3(d) or the guidelines for formulation patents set out in Correa's Guidelines on Patentability would ensure some certainty for the rejection of Abbott's subsequent applications. As a result, generic manufacturers capable of producing lopinavir in Brazil would have been permitted to do so. Alternatively Indian generic companies would have been in a position to supply Brazil given that neither lopinavir nor any of the follow-on type patents have been granted there.

With respect to lopinavir, the first patent covering the base compound was apparently filed in December 1995. As a result, under the 12-month priority rule, any patent filed in Brazil would have to have been filed in December 1996. Had Brazil not provided pipeline protection, the base patent of lopinavir would likely not have been filed in Brazil.

As with ritonavir, all key subsequent patents for lopinavir relate to either polymorphic forms, formulations or processes. Under rigorous patentability laws, the polymorph and formulation patents would likely not be granted. While the process patents may be considered new and

non-obvious, there would be scope for generic manufacturers to work around them.

In view of the above scenario, Brazil could currently be paying the lowest generic price of US\$440 per patient/year (or at least significantly less than Abbott's current price) for heat stable Kaletra.

## **V.2 Colombia's Request for a Compulsory License on Lopinavir/Ritonavir**

According to patent information made available and upon which the compulsory license request was based, the patent covers the base compound lopinavir and lopinavir in combination with ritonavir – but not ritonavir alone.

Under rigorous criteria for patentability, combining a compound with another known active ingredient (ritonavir) which does not show a new and non-obvious synergistic effect would not be considered patentable. In this case the claims in the Colombian patent covering lopinavir with ritonavir might not be patentable.

With rigorous patentability criteria subsequent patents for ritonavir would also be rejected. As described for Brazil, it would therefore mean that Colombia could at least source ritonavir from generic suppliers.

Although such a scenario would still leave the issue of the blocking patent for lopinavir, which would most likely be patentable even under strict patentability guidelines, any negotiating position with Abbott would be much stronger. This is because the most valuable element in the combination patent for heat stable Kaletra is ritonavir.

## **V.3 Malaysia's Compulsory License for Lamivudine/Zidovudine**

Patents for the base compounds lamivudine and zidovudine were apparently not filed in Malaysia as the first filing dates were 1985 and 1989, thereby pre-dating TRIPS.



In such a scenario, with no blocking patents for lamivudine and zidovudine, under rigorous patentability criteria the combination patent for lamivudine and zidovudine (Combivir) would not be considered patentable. This is because it is arguable that there is no synergistic effect between the two compounds, but simply a combination patent including inert excipients for formulation purposes.

Indeed, an application in India for the combination lamivudine/zidovudine was withdrawn by GlaxoSmithKline following a pre-grant opposition that showed the non-patentability of the combination.

## **VI. FINDINGS AND CONCLUSIONS**

Further research is necessary to determine whether patentability standards, if strengthened, could have eliminated the need for the more politically charged procedures related to compulsory licensing discussed in this chapter. However, our review of this issue demonstrates that in certain scenarios, on follow-on drug products in particular, rigorous patentability standards would have waived the need to adopt compulsory licensing.

India provides a useful model for the question of whether strengthening patentability criteria, and adopting related TRIPS flexibilities, can sidestep the politically controversial compulsory licensing mechanisms. India adopted two important features in its 2005 act that help us examine this question: section 3(d)'s efficacy test, and the section 11 "automatic compulsory license" provision. As a result of these and other important pre-emptive measures, compulsory licensing has not yet arisen as a high profile issue in India. However, as many of the third-line ARVs and newer drugs have been patented in India, despite section 3(d), India's Department of Industrial Policy and Promotion has started a process to address concerns relating to future access by way of compulsory licensing.

The political dynamics at play illustrate the complexities and feasibility of adopting either strategy. Older trade agreements








demonstrate that the US Government and others have attempted on multiple occasions to narrow compulsory licensing provisions. Much more insidious is the recent attempt by the U.S to incorporate restrictions within trade agreements on strengthened patentability criteria such as India's section 3(d), or procedural mechanisms that help with strengthening patent criteria, such as pre-grant opposition mechanisms.<sup>62</sup>









It is hoped that this case study provides a useful starting point for a very fertile area of research that could enable better understanding of the practical implementation of rigorous patentability criteria policies versus compulsory licensing.










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<sup>62</sup> Proposed U.S. IP Chapter for the Trans-Pacific Partnership Agreement (2011).

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PATENT SYSTEMS are generally viewed as a means to reward inventiveness, promote technical progress and foster the dissemination of innovations. However, the role of the patent system in promoting innovation is less substantial than often claimed, especially in developing countries. Patents may even stifle the very innovation they are supposed to foster and can be used to unduly block or delay legitimate competition. This is particularly the case in the pharmaceutical sector, where a large number of patents on developments with low or no inventive activity have been extensively used to deter generic competition. In some situations, governments have faced the need to grant compulsory licenses to overcome the limitations created by such patents. This book examines patent trends and the use of compulsory licenses relating to pharmaceuticals in five developing countries: Argentina, Brazil, Colombia, India and South Africa. It finds a number of common features and problems, and shows how the application of rigorous standards of patentability may contribute to protect public health by promoting local production and competition.

**Carlos M. Correa** is Special Advisor on Intellectual Property and Trade of the South Centre and Director of the Center for Interdisciplinary Studies on Industrial Property at the Law Faculty, University of Buenos Aires.



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