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challenges for public health

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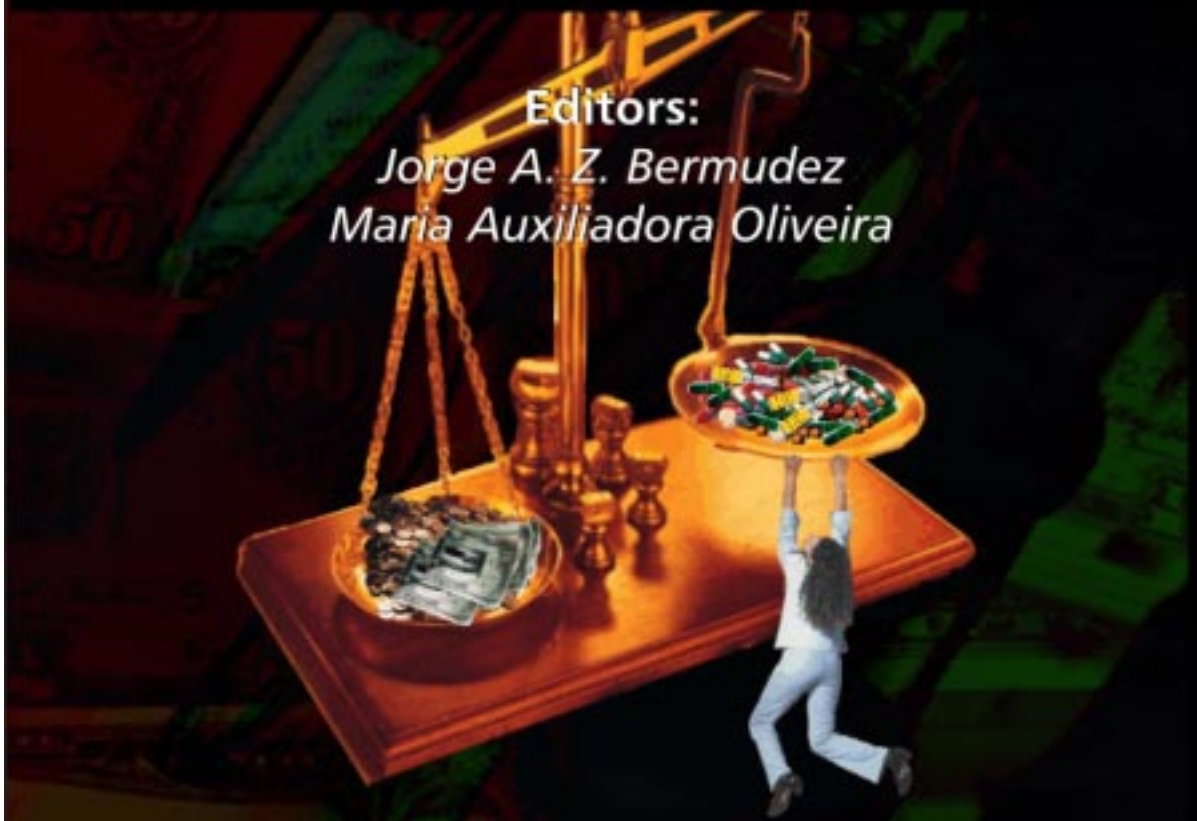

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SERGIO AROUCA

ENSP

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This book presents information produced or compiled by Nucleus for Pharmaceutical Policies professionals and external collaborators regarding the process of implementation of the TRIPS Agreement in developing countries, focusing on its implications for public health policies, particularly those related to access to medicines.

Interpretations and views expressed in this publication are solely the responsibility of the authors, not representing any official or institutional position, as to the issues here approached.

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Foreword

The Brazilian pharmaceutical market is one of the world's ten largest with a yearly income totaling close to US$ 10 billion and characterized by a high concentration of transnational companies, mainly when segmented by therapeutic class. Ministry of Health expenditures for four different categories of medicines represent one tenth of the total market value, equivalent to US$ 1 billion.

Examination of the implications of intellectual property rights on access to medicines is a recent development in the field of public health Not long ago, this topic was confined to economists and lawyers specializing in intellectual property. The 49th World Health Assembly, which was held in May 1996, changed this by bringing the consequences of globalization and trade agreements on access to medicines to the forefront. In that year the World Health Assembly adopted the "Revised Medicine Strategy" resolution to be incorporated into WHO medicines policy, which included gathering "information on the impact of the World Trade Organization on national policies for essential medicines". Following the adoption of the resolution, WHO's Essential Medicines Action Programme developed an action plan with the following points:

1. Identification of WTO agreements related to access to essential medicines and pharmaceutical policies, with subsequent notification to Member States of their existence.
2. Study of the implications of globalization on innovation, development, production, trade and prices of medicines; with the purpose of identifying possible negative effects that the TRIPS Agreement and/or other trade agreements have on access to essential medicines.
3. Notification of Member States on the need to adopt measures to protect public health.

There is no doubt that the adaptation and implementation process of the TRIPS Agreement has had an impact on the pharmaceutical sector as well as on access to medicines. Among the consequences, it is important to highlight the delay in introducing competing generic medicines to the market. In essence, patent protection creates a monopoly of exploitation rights for the patent owner. In the case of TRIPS, exclusive exploitation rights extend for twenty years. As

liberal economics has demonstrated, the lack of competition results in a lack of stimuli to lower prices, which therefore remain high and end up compromising public policies aiming to expand access to medicines. One cannot ignore the fact that the extension of monopoly rights for such long periods of time inhibits local production, even when countries have the industrial capacity.

In Brazil, discussion of the implications that trade agreements have on public health is firmly established in the government's agenda and has resulted in specific actions. I am sure that the countries in this region also welcome industrial policies that promote social justice and equity for their populations.

The government is taking action to help the pharmaceutical sector overcome its current external economic and technological dependence through investments and capacity building, with a special emphasis on the official network of public laboratories. Also, expansion of access will count on integrated actions and distribution decentralization. The recently inaugurated Popular Pharmacy Program (Programa Farmacia Popular do Brasil) represents a further step in the direction of ensuring access to low cost medicines.

Additionally, we have the fundamental concern of doing our best to reduce the costs of medicines within our National Health System (Sistema Unico de Saude). Its mandate include universal access to medicines. Nevertheless, it is still necessary to continue to thoroughly examine all possible alternatives to effectively meet social policy needs.

Publications such as this one bring to light background conflicts between social and economic policies and contribute to inform different groups of persons in a globalized world who need information to act with caution, maturity and directed towards the public good. This is not the first, nor the last publication in this genre. Whether you agree or not with the authors´ positions, these debates have definitely been inserted into the health agenda. This is, without doubt, the unquestionable contribution that we would expect from them.

Humberto Costa,
Minister of Health
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Center for Pharmaceutical Policies

The Center for Pharmaceutical Policy (NAF) – since 1998 a PAHO/WHO Collaborating Centre for Pharmaceutical Policies – is part of the Sérgio Arouca National School of Public Health, Oswaldo Cruz Foundation, Rio de Janeiro, Brazil. It is composed of professionals of the highest academic levels in different fields of knowledge such as Medicine, Pharmacy, Sociology, Social Work and Biology, with experience in health services and advocacy.

NAF has been working in permanent interaction with the three levels of government in Brazil, and in constant collaboration and interchange with the Health Technology and essential medicines programs of PAHO and WHO. Its global references for planning activities come from the WHO Department of Essential Drugs and Medicines Policy, PAHO Essential Drugs and Technology Program, and the Brazilian National Drug Policy.

The Center has been participating in the processes of formulation, implementation and evaluation of Pharmaceutical Policies in the context of Health Reforms in the Americas and in Portuguese and Spanish-speaking countries around the world, development of research and elaboration of documents, books, and papers; organization of regional courses for policy-makers, meetings, seminars and other international events, teaching at post-graduate public health courses, development of collaborative studies at national and regional levels, adaptation and translation to Portuguese of specific WHO reference documents and development of activities aiming to improve access to care for PLWHA.

NAF's initial activities included: participation in the Brazilian National Drug Policy formulation (1998), coordination of the Essential Drugs List review in 1998 (published 2000), production of the National Therapeutic Formulary, 2000, evaluation of health programmes such as the National Evaluation of the Basic Pharmacy Programme, 1998-1999 (Medicines for Primary Health Care), evaluation of the Pharmaceutical Services in the State of Rio de Janeiro and Pharmaceutical Services and access to Antiretrovirals in the City of Rio de Janeiro.

Recent activities are the Pharmacological and Clinical Bases for Currently Used Medicines in Brazil, 2002, support to ANVISA (Brazilian National Regulatory Agency for Health) for the definition of priorities for generic medicines, seminars,

and a broad range of educational activities in Rational Use of Medicines, translation of the Teacher's Guide to Good Prescribing and the 12th Revision of the WHO Model List of Essential Medicines, development of the Brazilian Hospital Pharmacies Evaluation (phase I) .

Research and Post-graduate studies and projects include: Overview of the Brazilian pharmaceutical industry, National Drug Policy in the context of Colombian Health Reform, Brazilian Hospital Pharmacies Evaluation (phase II), Evaluation of Pharmaceutical Services in Primary Health Care (Case study), High-cost drugs in Brazil. Are they Essential Drugs?, Evaluation of mechanisms and indicators of access to Essential Drugs in Brazil, Financing AIDS care in Latin American and Caribbean Countries, Monitoring the process of implementation of the TRIPS Agreement in Latin American and Caribbean countries, Brazil Pharmaceutical Situation (PAHO/WHO), National Evaluation of the HIV/AIDS Pharmaceutical Services Program, Development of a Methodology for Monitoring Medicines Market.

Participation in international initiatives including PAHO-World Bank-IDB (Shared Agenda): Pharmaceutical Clearinghouse for the Americas, Millennium Project (UNDP) – Aids, TB, Malaria, and Access to Medicines Task Force, Médecins sans Frontières: Drugs for Neglected Diseases (DNDi), Management Sciences for Health (Joint WHO-MSH): Development of a Methodology for Evaluating Access to Drugs in Developing Countries (SEAM Study), Health Action International (Joint HAI-WHO): Development and Testing a Methodology for Comparative Studies on Drug Prices in Developing Countries, WHO: Network for Monitoring WTO Trips Agreement and the Access to Essential Medicines, Global Fund PSM-Advisory Panel.

Since 2002 NAF has been hosting the Secretariat of the Global Care Financing Network for PLWHA, a jointly initiative with UNAIDS and the French Ministry of Foreign Affairs.

NAF has also undertaken projects of multilateral collaboration, in NDP with Angola (1998), Honduras (1999), Comparative Drug Prices (Mexico, Brazil, Argentina), Health Care Financing and Access to Antiretrovirals in Latin America: case studies of Argentina, Bolivia, Brazil, Colombia and Honduras.

Other relevant recent initiatives include participation in the Brazilian Transition Government period of 2002: Pharmaceutical Policies Working Group (including economic regulation and access to medicines), the new structure of the Ministry of Health (the Secretariat for Health, Technology and Essential

Supplies), advisory activities substantially enhanced with the Ministry of Health, close interaction and follow-up on cooperation enacted by the Brazilian HIV/ Aids Programme and joint international proposals (TRIPS Agreement monitoring and Doha Declaration). The NAF coordinator, Dr. Jorge Bermudez, currently Director of the National School of Public Health has also been actively participating, as part of the Brazilian delegation, in the last four World Health Assemblies (2000-2004) and in the recent meetings of the WHO Executive Board.

Jointly with PAHO and WHO, NAF has organized three international seminars: The I International Seminar: Medicines in the context of the Health Reform: Looking for Equity, 1998 (58 participants, 16 countries), The II International Seminar: Drug Policy, Equity and Access, 2000 (61 participants, 10 countries) and The III International Seminar on Access to Drugs: Fundamental Right of the Citizen and Duty of the State. 2002 (54 participants, 18 countries). Jointly with UNAIDS and the French Ministry of Foreign Affairs NAF has also organized three Satellite Meetings: (1) "Financing Care in Latin America and The Caribbean: Options for Large-Scale Programs", Havana, Cuba April 2003; (2) "Opportunities for Reaching 3 million people with ARV treatment by 2005, Dakar, Senegal, December, 2003, (3) "From Barcelona to Bangkok: Financing Treatment and Care to Reach 3 by 5", Bangkok, Thailand, July, 2004.

The present publication presents information produced or compiled by NAF professionals and external collaborators regarding the process of implementation of the TRIPS Agreement in developing countries and its implications for public health policies, particularly those related to access to medicines in developing countries.

It intends to be a contribution to health sector professionals´ better understanding of the WTO TRIPS Agreement and Public Health, especially regarding the implications for access to care and to medicines in the developing world.

Table of Content

Abbreviations and Acronyms

ABIFARMA – Brazilian Transnational Pharmaceutical Companies Association

ANVISA – National Health Surveillance Agency

ARIPO – African Region Industrial Property Organization

ARV – Antiretroviral

CEME –Central Medicines Agency

CIPIH – Commission on Intellectual Property Rights, Innovation and Public Health

CL – Compulsory License

CMS – Medicare Centres and Medicaid Services

Conass – National Council of State Health Secretaries

Cptech – Consumer Project on Technology

CUP – Convention of the Paris Union

DCB – Brazilian Non-Proprietary Name

DFID – UK Department for International Development

DSU – WTO Dispute Settlement Understanding

EB – Executive Board

EDL – List of Essential Medicines

EDM – WHO Department of Essential Drugs and Medicines Policy

FARMANGUINHOS – Institute of Technology in Medicines

FDA – Food and Drug Administration

FFOE – College of Pharmacy, Dentistry and Nursing

FTA – Free Trade Agreements

FTAA – Free Trade Area of the Americas

FTC – US Federal Trade Commission

FUNED – Ezequiel Dias Foundation

FURP – Foundation for Popular Medicines

GATS – General Agreement on Trade in Services

GATT – General Agreement on Tariffs and Trade

GI – Gastrointestinal

GSK – Glaxo Smith Kline

HAART – Highly Active Antiretroviral Therapy

HAI – Health Action International

HMOs – Health Maintenance Organizations

IMDs – Incrementally Modified Drugs

IMF – International Monetary Fund

INN – International Non-Proprietary Name

INPI - National Institute for Industrial Property

IPR – Intellectual Property Rights

IQUEGO – State Chemical Company of Goiás

IVB – Vital Brazil Institute

LAFEPE – State Pharmaceutical Laboratory of Pernambuco

LAFERGS – Pharmaceutical Laboratory of Rio Grande do Sul

LAFESC – Pharmaceutical Laboratory of Sta. Catarina

LAQFA – Air Force Chemical and Pharmaceutical Laboratory

LEPEMC – Laboratory of Teaching and Research in Medicines and Cosmetics

LFM – Navy Pharmaceutical Laboratory

LIFAL – Pharmaceutical Laboratory of Alagoas

LIFESA – State Pharmaceutical Laboratory of Paraíba

LPM – Medicines Production Laboratory

LQFE – Army Chemical and Pharmaceutical Laboratory

LTF – Pharmaceutical Technology Laboratory (UFPB)

Medicines Act – South African Medicines and Related Substances Control Amendment Act

MoH – Ministry of Health

MSF – Doctors Without Borders (Medicins sans Frontières)

NDAs – New Drug Applications

NDP – National Drug Policy

NGO – Non-Governmental Organization

NIC – Newly Industrialized Countries

NIH – National Institutes of Health

NIHCM – National Institute of Health Care and Management

NME – New Active Entities

NOB – Basic Operational Norm

NSAIDs – Non-Steroidal Anti-Inflammatory Drugs

NUPLAN – Center for Research on Food and Medicines (RN)

OAPI – Organization of Intellectual Property

OECD – Organisation for Economic Co-operation and Development

PBS – Pharmaceutical Benefits Scheme

PFB – Basic Pharmacy Program

PhRMA – Pharmaceutical Research and Manufacturers of America

PLWHA – People Living with HIV/AIDS

PMA – Pharmaceutical Manufacturers' Association of South Africa

Pró-Genéricos – Brazilian Generic Medicines Industry

PTO – US Patent and Trademark Office

R&D – Research and Development

RDS – Revised Drug Strategy

RENAME – National List of Essential Medicines

RPI – Industrial Property Magazine

SADAP – South African Drug Action Programme

SNVS – National Sanitary Surveillance System

SUS – Unified Health System

TRIPS Agreement – Agreement on Trade Related Aspects of Intellectual Property Rights

TRIPS Council – WTO Council for TRIPS

TT – Technology transfer

UNAIDS – United National Joint Program on HIV/AIDS

UNDP – United Nations Development Program

UNICEF – United Nations Children's Fund

USTR – United States Trade Representative

Waxman-Hatch Act – US Drug Price Competition and Patent Restoration Act

WB – World Bank

WHA – World Health Assembly

WHO – World Health Organization

WIPO – World Intellectual Property Organization

WTO – World Trade Organization

Part I – Intellectual Property Rights and Public Health

Chapter 1

Intellectual Property in the Context of the WTO TRIPS Agreement: What is at Stake?

Jorge A. Z. Bermudez, Maria Auxiliadora Oliveira & Gabriela Costa Chaves

Introduction

The most extensive negotiation round of the General Agreement on Tariffs and Trade (GATT) was the Uruguay Round, which ended in the signing of a series of multilateral trade agreements in April 1994, including the Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS Agreement). This Agreement addresses, among others, the subject of patents and establishes that all Member States of the World Trade Organization (WTO)-created in January 1995-should grant patents for inventions in all technological fields, including pharmaceutical products and processes.

A patent is considered an instrument of economic policy that, depending upon the country, can reap benefits or not. It is argued that patents stimulate investment in scientific and technological development, producing innovations and benefits for society. In fact, in the last 50 years the development of new medicines has been highlighted as an important determinant of increasing the quality of life and life expectancy of large percentages of the world's population.

However, despite stimulating innovation, patents by their nature create monopolies, which in turn allow pharmaceutical companies to establish and implement high prices for a minimum period of 20 years (as established in the TRIPS Agreement). One consequence is the delay in commercialization of generic versions of medicines[1], which offer more affordable prices especially for poor populations.

[1]The concept of a generic medicine varies among policy agreements and national regulations. For example, while Brazil, the United States and Canada require a bioequivalence test to approve generic medicines, most developing countries do not.

Although access to medicines is the result of many different dimensions, which range from service organization to patient adherence to treatment, medicine prices are one of the essential components because they have a direct impact on affordability for governments and individuals. For this reason, the implementation of the TRIPS Agreement was discussed and negotiated in many national and international forums related to public health.

The first time the theme of trade agreements entered into the health agenda was during the 49th World Health Assembly (WHA) in 1996. Since then, various governmental, non-governmental and international organizations have been developing initiatives aiming to maximize the positive effects and minimize the negative effects of the TRIPS Agreement on access to medicines for populations in developing and least developed countries.

This chapter discusses aspects of the TRIPS Agreement related to public health and identifies the principal actors involved in the negotiations and their interests as well as debates that emerged from the implementation process - starting in January 1995. It describes the outcomes of several negotiations in international arenas.

The chapter is organized into six topics. The first two present a conceptual and brief historical process of the organization of the international system of intellectual property. The third describes and discusses the principal characteristics of the TRIPS Agreement, pointing out the mechanisms and flexibilities that can favor drug policy implementation. The fourth and fifth topics describe, from a historical perspective, the debates and negotiations about the implications of the TRIPS Agreement on public health, which have been on going since 1995. Relevant actors and interests involved are also described, as well as their achievements. For the section on final considerations, the authors reflect upon the challenges that will be faced by these different actors in the coming years.

Intellectual Property and Industrial Property: from the Paris Convention to WIPO

Intellectual property is a generic expression involving the rights individuals hold over their own creations, work and production, based on intellect, talent and skill. Intellectual Property covers two broad areas: Copyright and Industrial Property. The first area protects literary, artistic, photographic, cinematographic works and software. Industrial Property is a collective term for

a set of rights related to an individual's or company's industrial or commercial activities, such as: use of trademark, geographical indications, industrial designs, patents, layout-designs (topographies) of integrated circuits and protection of undisclosed information (Bermudez *et al.*, 2000a).

The first Patent Law known in history was approved in 1474, in Venice, and granted the inventor exclusive rights to produce their invention for a limited period. Nevertheless, when a new product was placed in the market, it received insignias, emblems and other identifying marks that permitted merchants to control distribution of goods and to keep a portion of surplus value generated by production for themselves. Since the producer, in this context, was unable to maximize profits, strategies were developed to guarantee control over the product commercialization chain. Thus the modern trademark system emerged.

After the Industrial Revolution, in the 19th century, international regulations for Industrial Property arose when manufacturers had already gained greater control over production and distribution of their inventions through systems of patents and trademarks. Before the 19th century, no international system of industrial property existed. Each country had autonomy to define their legislation. Therefore, an invention under patent protection in one country could be used by another without violating any laws.

In 1883, several countries (Brazil included) signed the famous Paris Union Convention (hereafter referred to as Paris Convention) whose three basic premises operate the International Industrial Property system:

(1) Independence of patents and trademarks[2];

(2) Equal Treatment for Nationals and Foreigners[3];

(3) Priority Rights[4] (Bermudez *et al.*, 2000a).

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[2] Independence of patents and trademarks means that granting a patent in one country bears no relationship to granting it in another.

[3] In the area of national legislation for Industrial Property, Equal Treatment for Nationals and Foreigners bars any sort of preferential treatment or discrimination that favors national interests.

[4] The priority rights concept means that parties filing a claim to a patent, utility model, industrial model or design, or industrial, commercial, or services trademark in one of the Patent Union countries, or their successors, have the right to file the same claim in other signatory countries with priority rights under the time frames established by the Convention.

The signatory countries of the Paris Convention believed that an international industrial property system would enable the creation of production centers into different regions of the world. Thus, new technology could be exploited through the use of qualified local labor and through better access to raw materials, resulting in quality products at lower prices (Barbosa, 2003).

The Paris Convention, signed in 1883, has been revised eight times: 1886 Rome, 1890-1891 Madrid, 1987-1900 Brussels, 1911 Washington; 1925 the Hague; 1934 London; 1958 Lisbon; 1967 Stockholm (Gontijo, 2003). This Convention survived both World Wars as well as the creation of the World Trade Organization (WTO) in 1995 and presently is in force (Barbosa, 2003).

In 1884, Paris Convention established an international office to conduct administrative procedures. In 1886, with the Berne Convention in force, -which had the objective of protecting literary and artistic works-, another international office was created. In 1893, a merger occurred between these two offices and resulted in the creation of the Unified Office for the Protection of Intellectual Property, more commonly known as BIRPI (Bureaux Internationaux Réunis pour la Protection de la Propriété Intellectuelle). In 1970 the BIRPI gave rise to the World Intellectual Property Rights Organization (WIPO), headquartered in Geneva (WIPO, 2003).

After the Second World War, a new global economic order was established and new international organizations were created. Through multilateral agreements, these organizations mediated relations between nations. The International Monetary Fund (IMF) and the World Bank (WB) were both institutionalized in 1944, and their initial objectives were to manage the international monetary system and to finance projects that could reconstruct the economy of European countries devastated by the war. Additionally, it is important to highlight the creation of the General Agreement on Tariffs and Trade (GATT) in 1947. The importance of GATT extends beyond that conferred to a mere treaty; it was a milestone for multilateral negotiations aiming to diminish international trade barriers.

GATT was not considered an organization; therefore, countries that abided by the agreement were referred to as contracting parties. They had the following obligations (1) to concede Most-Favored-Nation[5] treatment to all other parties,

[5] The Most Favored Nation treatment-existent in the GATT and also incorporated in the TRIPS Agreement-means that the WTO signatory countries can not give differential treatment to goods coming from different exporting countries. In other words, any advantage given to a country's product should be conceded to all WTO Member States (Velasquez & Boulet, 1999; Barbosa, 2003).

(2) to grant tariff concessions to all other parties, and (3) to not take measures that would result in obstacles to international trade. These measures allowed the GATT to achieve its objective of "...reducing customs duties and other barriers to trade and eliminating all discrimination in international trade." (Velásquez & Boulet, 1999:10).

It is worth mentioning that the GATT fostered a series of multilateral trade negotiation rounds, which represented important steps towards organizing international trade. During the period from 1947 to 1961, the rounds played an important role in the reduction of custom duties. The Kennedy Round (1964-1967) led to a further decrease in customs duties and the negotiation of an agreement on anti-dumping practices. The Tokyo Round (1973-1979), formalized a series of agreements regarding: (1) technical barriers to trade (2) government procurement (3) subsidies (4) customs valuation (5) import licenses (6) anti-dumping practices.

The most extensive negotiation round was the Uruguay Round, which lasted from 1986 to 1994 and culminated in the creation of the World Trade Organization (WTO).

From GATT to the World Trade Organization

The 1980s were marked by a new reality of international trade, in which the GATT rules were no long adequate. After the economic crises of the 1970s, the world was shaken up by a profound capitalist reform, supported by the informatics and communications revolution. Therefore, it became possible to integrate spatially decentralized productive processes. New technology influenced all economic sectors. For example, it revolutionized the financial system by enabling simultaneous electronic connections between different markets (Vieira, 1997).

At the same time, privatization, deregulation and increased flexibility of markets intensified international competition for private capital. In this context, as Viera (1997) remarked, a new set of phenomena occurred: (1) increasing unification of national and international finance markets into one source of rapidly moving capital; (2) accelerated formation of regional economic blocks (3) transnational mergers and acquisitions; and, (4) the need to coordinate the

largest national economies, expressed by the creation of the G7. This new spatial configuration of the world economy came to be known as Globalization.

In the same period, Japan, along with some Asian countries (the New Industrialized Countries[6]), gained competitiveness in the field of technology through clever use of the intellectual property system. Thus, it was possible to note a considerable loss of technological leadership by the United States that, as a short term measure, launched a unilateral offensive and imposed trade sanctions onto countries that did not conform to the parameters they defined as acceptable (Barbosa, 2003).

The Uruguay Round was organized to discuss issues related to international trade and, due to pressure from the United States, other areas such as services and intellectual property rights (IPR) were discussed. This round stands out from those held previously because of the efforts made to harmonize national trade policies related to protection of intellectual property. In practice, this Round affected a series of national economic and trade policies that define competition rules within countries (Correa, 1997).

It is important to remember that in 1986, when the Uruguay Round began, the majority of developing countries did not grant patents for pharmaceutical products. However, over the years this situation changed substantially within the context of State reform processes, implemented in the majority of these countries. Changing the rules governing intellectual property rights was one of the requirements imposed onto developing countries in bi-lateral trade agreements with developed countries (Tachinardi, 1993; Correa, 1997).

The end of negotiations occurred in April 1994 in Marrakech, Morocco with the signing of a series of trade agreements to be administered by a new organization-the World Trade Organization (WTO). This organization began to function in January 1995, in Geneva, acting as an organ of the United Nations, counting 147 Member States as of April 2004 (WTO, 2004).

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[6] There are Asian and Latin American NICs, such as Korea, Taiwan, Singapore, Hong Kong, Brazil, Argentina and Mexico.

WTO responsibilities are:

1. Administration of the new multilateral trade agreements;
2. Provision of a forum for fresh negotiations;
3. Settlement of disputes;
4. Surveillance of national trade policies;
5. Cooperation with other international bodies in drawing up of economic policies at the global level.

Despite also including sectoral or plurilateral agreements, only multilateral agreements are obligatory for WTO Member States. Besides the multilateral agreements related to trade in goods are the General Agreement on Trade in Services (GATS) and the TRIPS Agreement.

Since the WTO was created in 1995, WIPO has no longer been the principal institution sponsoring discussions and negotiations of agreements on the subject of intellectual property. Thus, it focuses only on the practical aspects of implementation of the new system. Nevertheless, there is a movement within WIPO to maintain its importance, in spite of TRIPS (Gontijo, 2003).

Chart 1 contains summaries of the main differences between the WTO and the GATT (Velásquez & Boulet, 1999).

CHART 1: Main differences between the GATT and the WTO

	GATT	WTO
Nature	Multilateral agreement, without an established organizational structure that counts on an *ad hoc* secretariat	It is a permanent institution.
Mandate	The agreement was applied on a provisional basis.	The mandates are permanent.
Scope of rules	All norms applied to trade in goods.	All agreement norms apply to trade in goods, services and also aspects of intellectual property rights related to trade.
Type of Agreements	Originally multilateral, but during the 1980s, a series of optional plurilateral agreements were added.	The majority of agreements are multilateral, and all Member States must abide.
System for the settlement of disputes	Slow and susceptible to blockages	Fast and automatic, and dispute settlement decisions are better assured.

Source: Adapted from Velásquez & Boulet, 1999.

The TRIPS Agreement: Principal Characteristics

The TRIPS Agreement is divided into seven parts composed of 73 articles. Part II contains the most important elements for Public Health, especially in relation to access to medicines. The matters covered in this section include: (1) copyright and related rights, (2) trademark, (3) geographical indications, (4) industrial designs, (5) patents, (6) layout-designs (topographies) of integrated circuits and (7) protection of undisclosed information (8) control of anti-competitive practices in contractual licenses.

The TRIPS Agreement defines minimum standards in the field of intellectual property rights that the WTO Member States must incorporate into their legislation. More restrictive legislation can be implemented, provided that such legislation is consistent with the provisions of the TRIPS Agreement, as stated in Article 1. Two important aspects should be highlighted from this Article. First, the TRIPS Agreement rules set minimum standards for protection of intellectual property rights. Second, the Agreement must first be incorporated into national legislation, before it is enforced at national level (Barbosa, 2002).

Article 7 establishes the objectives of the TRIPS Agreement, emphasizing that, "The protection and enforcement of intellectual property rights should contribute to the promotion of technological innovation and to the transfer and dissemination of technology, to the mutual advantage of producers and users of technological knowledge and in a manner conducive to social and economic welfare, and to a balance of rights and obligations."

Article 8 defines the principles of the TRIPS Agreement, which include the right of Member States to:

(1) adopt the measures necessary to protect public health and nutrition, and to promote the public interest in sectors of vital importance to their socio-economic and technological development, provided that such measures are consistent with the provisions of this Agreement.

(2) defend themselves against the abuse of intellectual property rights by right holders or the resort to practices which unreasonably restrain trade or adversely affect the international transfer of technology.

Before the TRIPS Agreement, the Paris Convention signatory countries could opt to extend or exclude patent protection for some technological fields,

recognizing national autonomy to define the best strategy for social and economic development. After January of 1995, WTO Member States were required to comply with TRIPS, which meant granting protection to all technological fields, except for the exceptions stated in Article 27[7].

Consequently, countries lost the autonomy to choose the patent protection regime that would best benefit their social, economic and technological development. This happened because developing and least developed countries were obligated to abide by the minimum requirements of the TRIPS Agreement, which include granting patents for products and pharmaceutical processes essential for health policy implementation.

The protection of property rights includes: (1) products, (2) processes and (3) uses. A patent holder is guaranteed exclusive rights of exploitation for a period of time, a competitive advantage. It is argued that patents provide incentives for research and development (Barbosa, 2002). However, this occurs only when the patented product gains market share, which means that research is mainly driven by market forces (MSF, 2002).

It is important to note that the industries of the chemical and pharmaceutical sector are most in need of patent protection because their products are easily copied. Thus, a patent guarantees financial return for investments in research and development (Sherer & Watal, 2001; Benkimoun, 2002; Mansfield, 1986). However, patents for medicines can be contradictory in nature, since these products can save lives. In other words, the monopoly conferred by a patent allows the pharmaceutical industry to establish high prices, which consequently can affect access to medicines (Oliveira *et al*., 2004). According to statements from national drug policy program managers from

[7]There are exclusions allowed to patentability for reasons of public order, moral grounds - including protecting human life or public health, animal or vegetable, or to avoid serious damage to the environment. Surgical methods- therapeutic or diagnostic- are also excluded, so are essentially biological processes, plants and animals, except for microorganisms (Bermudez *et al*, 2000).

Latin America and the Caribbean[8], prices constitute one of the most significant barriers to access medicines, especially among the poorest populations. On the other hand, as described in the CIPR[9] report on intellectual property and development policy (2002), there are technical problems in establishing a causal relationship between patents and drug prices. According to the authors, prices are influenced by other conditions such as: purchasing power, existence of competition, market structure, responsiveness of demand to price, governmental price controls and regulations (CIPR, 2002). The issue of medicine prices has been intensely debated in several national and international forums, and as a result, the subject of trade agreements and public health has been incorporated into the health agenda (WHO, 1996; WHO, 1999; UN, 2001).

Since the TRIPS Agreement treats medicines as any other good, it can potentially have a negative impact on access to medicines, especially in developing and least developed countries (Velasquez & Boulet, 1997; T'Hoen, 2002, Supakankanti *et al.*, 2001; Bermudez *et al.*, 2000a e Correa, 2000).

In order to minimize negative effects of patent protection on access to medicines, the TRIPS Agreement allows countries to adopt flexibilities and safeguards to protect public health. Chart 2 presents the main TRIPS Agreement provisions related to drug policy.

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[8] In April 2003, in Havana, Cuba the Satellite Meeting entitled, "Financing Care in Latin America and the Caribbean: Options for large scale programs" took place, during which some managers of national drug programs for HIV/AIDS treatment in Latin America and the Caribbean emphasized the importance of price in relation to access. Francisco Rossi, coordinator of the ARV access program in Colombia, stated that despite the existence of other determinant factors, price, without a doubt, is the most important factor involved. Price requires a large portion of resources, which could be utilized for other actions considered necessary in an integral approach to control the epidemic (Rossi, 2003).

[9] The *Commission on Intellectual Property Rights*(CIPR), created by the United Kingdom Department for International Development, examined how national IPR regimes could be better designed to benefit developing countries.

CHART 2: TRIPS Agreement provisions that favor health policy implementation

PROVISIONS	TRIPS AGREEMENT ARTICLE	DEFINITION
Transition period to adapt national legislation to the TRIPS Agreement	Art. 65 Transitional arrangements Art. 66 Least developed countries	Since January 1995 WTO Member countries have had the following deadlines to modify their national legislation: 1. Developed countries: 1 year until Jan/1996 2. Developing countries: 5 years until Jan/2000 3. Least developed countries: 11 years until Jan/2006.
Transition period to recognize patents in technological sectors not protected before the TRIPS Agreement. (For example, patent protection in the chemical sector of various countries.)	Art. 65.4	Developing countries have an additional 5 year period (until 2005) to recognize patents in the above referred to sectors. Note: The Ministerial Doha Declaration on TRIPS Agreement and Public Health (WTO, 2001) established in paragraph 7 that least developed countries could extend the transition period for pharmaceutical products and processes until 01/01/2016.
Parallel imports or exhaustion of rights at regional and/or international levels.	Art. 6 - Exhaustion of rights	"Parallel" imports involve the import and resale in a country, without the consent of the patent holder, of a patented product which was put on the market of the exporting country by the title holder or in another legitimate manner (Correa, 2000:71).
Bolar Exception (*early working*)	Art. 30 Exceptions to Rights Conferred	This exception allows a company to complete all the procedures and tests necessary to obtain market approval for a generic product, before the original patent expires (Correa, 2000).
Compulsory Licensing	Art. 31 Other Use Without Authorization of the Right Holder	Allows exploitation of a patented object, without patent holder consent through government authorization, but with remuneration.

Sources: Velásquez & Boulet (1999), Correa (2000) e Bermudez *et al.* (2000a).

As described in Chart 2, the transition period for patent protection in the pharmaceutical sector could be used so as to permit developing countries to build local industry. Consequently, countries could be more competitive in the market, while at the same time diminishing external economic and technological dependence, a typical characteristic of developing countries' pharmaceutical sectors (Bermudez, 1995).

It is important to point out that many developed countries only granted patents for medicines after building their national industries (Bermudez, 1992). India opted to utilize the full transition period to strengthen local technological capacity. This has enabled the development and consolidation of infrastructure for research and development as well as manufacturing capabilities, which has allowed India to conquer a greater international market share. One important result of this policy has been the ability to market medicines, such as those needed to treat HIV/AIDS. These generic versions are available at significantly lower prices than those offered by patent holding transnational companies in other countries (Morrison, 2003).

The parallel imports flexibility represents an important pro-competition tool to promote access to lower-cost medicines. This tool aims to take advantage of current differential pricing practices used in several countries. There is no violation of the TRIPS Agreement because the patent holder's right was already exhausted in the country where the product was originally commercialized at a lower price.

In Brazilian patent law, the international exhaustion of rights (parallel imports) is allowed under compulsory licensing, as established in article 68 of Law #9.279/96 (Brasil, 1996) and in article 10 of Decree #3.201/99 (Brasil, 1999). The 1999 Decree regulates when and how a compulsory license can be issued in the case of national emergency or public interest. In 2003, some of these articles were modified by Decree # 4.830/03 (Brasil, 2003). The new version of article 10 changed the rules related to parallel imports. After issuing a compulsory license, Brazil can import the protected invention from any country where the invention has already been put on the market by the patent holder or with the patent holder's consent. The new version of article 10 now permits importation of the invention from a country where it is not under patent protection. In practice, this permits importation of products from countries that are still using

the transition period to grant patents for pharmaceutical products and process, such as India.

The Bolar exception allows immediate marketing of generics after patent expiration, thus promoting competition with the innovator medicine, which can lower prices. As stated by Creese & Quick (2001) competition is probably the most powerful policy instrument for the reduction of drug prices, when the patent has already expired. In the United States, when a patent expires and there exists just one competitor, the average wholesale price drops to 60% of the reference drug price, and when there exists 10 competitors, the price falls to 29%. For example, Canada has extensively used this provision for decades to strengthen its national technological capabilities and industrial base to produce generic drugs, consequently increasing access to medicines for its population (Reichman & Hasenzahl, 2002).

Compulsory licensing (CL) is considered an essential element of health-sensitive industrial property legislation, especially if the country does not have strong anti-trust legislation like the United States. A CL is an important tool in public policy for all WTO Members because it promotes competition, facilitates reduction of prices and compensates the patent holder for use of the invention (CIPR, 2002; NIHCM, 2002; Abbott, 2002). The grounds for issuing a compulsory license under TRIPS Agreement are described in Chart 3.

CHART 3: Grounds for issuing a compulsory license

GROUNDS FOR ISSUING A COMPULSORY LICENSE	DEFINITION
Failure to exploit or exploit on reasonable terms	A CL can be issued when a patent has not been locally exploited within a period of three years from the date of its original concession.
Public Interest	A CL can be issued when public interests prevail over the individual interests of the patent holder. Public interest does not necessarily have to be at the national or federal level, it could come from any sphere of government. This condition is consistent with article 31 of the TRIPS Agreement and can be applied in situations that fit the principles established in article 8.
National Emergency	A CL can be issued to respond to a national emergency, whether it is public or collective interest.
Remedy Anti-Competitive Practices	A CL can be issued to remedy anti-competitive practices, such as cartels and dumping.
Failure to obtain license under reasonable terms	A CL can be issued when voluntary permission has not been obtained to exploit the patent.
Lack of Local Production	According to article 5 of the 1967 Stockholm version of the Paris Convention, lack of local production can be grounds for issuing a CL (this issue is further discussed in the next section)
Dependent Patent	When there is an intermediate product or process that is patented and essential to produce the licensed invention, then, it is necessary to issue a CL for the intermediate product or process (dependent patent).

Source: Adapted from Correa, 2000; Barbosa, 2003.

The power of CL can be illustrated by the Brazilian example. In 2001, Brazil threatened to use the CL mechanism in order to obtain price reductions of four antiretroviral medicines (ARV), (Bermudez & Oliveira, 2002). It is important to highlight the role played by the public pharmaceutical laboratories, which have been essential for the implementation of national drug policy in Brazil (ALFOB, 2002). In the price negotiations mentioned above, involving the Brazilian government and three transnational pharmaceutical companies (Merck & Co, Inc., Roche and Abbott), the Instituto de Tecnologia de Fármacos/Oswaldo Cruz Foundation/Ministry of Health (Farmanguinhos) was able to provide reference prices to the Ministry of Health. Also, Farmanguinhos has the capacity to reverse engineer some patented ARVs. Therefore, the government was able to threaten to issue a CL in the case of a deadlock. The negotiation resulted considerable price reductions: 64.8% for Indavir, 59% for Efavirenz, 46% for Lopinavir/ritonavir

and 40% for Nelfinavir, thereby allowing sustainability of the national AIDS program[10].

In 29th October 2003, the Malaysian Government issued a Compulsory Licence to import the following antiretrovirals from the Indian company CIPLA: didanosine 100 mg and 25 mg tablets; zidovudine 100mg capsule; lamivudine 150mg+zidovudine 300mg tablet. In 5th April 2004, Mozambique also issued a Compulsory Licence (01/MIC/04) to the company Pharco Mozambique Ltda., which presented a project for local production of a triple compound of lamivudine, stavudine and nevirapine.

In the past decades, the United States and Canada have frequently used compulsory licensing in different technological fields, including drugs. The Canadian case is particularly emblematic because its extensive use of compulsory licensing for drugs led to the development of a domestic generic drug industry (Reichman & Hasenzahl, 2002).

For the health sector, it is particularly important to analyze the reforms of intellectual property legislation. This is because these regulations define patentable subject matter, exceptions to exclusive rights and flexibilities and safeguards applied in the pharmaceutical industry and other health technologies.

According to Correa (2000), health-sensitive industrial property law must include all flexibilities and safeguards allowed under TRIPS, for example, inclusion of international exhaustion of rights (parallel imports), Bolar exception as well as many conditions which allow a compulsory license to be issued. It is also important that countries use the full transition period for legislation reform. The incorporation of TRIPS flexibilities and safeguards are not mandatory but are essential to minimize negative impacts on health policy from patent protection. As stated by the author, legislation sensitive to public health needs enables governments to act efficiently in national emergencies and in situations involving public interest.

Thorpe (2001), Keyla (2003) and Oliveira *et al*. (2004) analyzed industrial property legislation of WTO Member States in Africa, Asia and Latin America and

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[10] A similar process of price negotiations for three ARVs has just ended (2003). In 2003, these ARVs were responsible for 63% of the Ministry of Health's ARV expenditures, close to US$120 million.

the Caribbean. These three studies examined the incorporation of the TRIPS Agreement provisions into national IPR legislation. The countries studied were: Argentina, Brazil, Mexico, the Andean Community (Bolivia, Colombia, Ecuador, Peru and Venezuela), Honduras, Panama, the Dominican Republic, India, Indonesia, Thailand, Sri Lanka, Member States of the African Intellectual Property Organization (Benin, Congo, Guinea, Nigeria, Burkina Faso, Ivory Coast, Equatorial Guinea, Mali, Chad, Central African Republic, Gabon, Mauritania, Togo) and Members of the African Regional Industrial Property Organization (Botswana, Lesotho, Somalia, Uganda, Gambia, Malawi, Sudan, Zambia, Ghana, Mozambique, Swaziland, Zimbabwe, Kenya, Sierra Leone, Tanzania). The results demonstrated that these countries did not fully incorporate all the TRIPS flexibilities and safeguards, which could enable them to achieve better public health outcomes.

The TRIPS Agreement and the global health agenda: who are the actors involved?

The 49th World Health Assembly (WHA) in 1996 was the first health related event in which the potential consequences on access to medicines from globalization and international trade agreements were discussed. In same year, WHO Medicines Strategy Resolution mandated the WHO to report on the impact of the work of the WTO with respect to national drug policies and essential drugs and make recommendations for collaboration between WTO and WHO, as appropriate. Consequently, the WHO Action Programme on Essential Drugs developed a strategic plan with the following objectives:

(1) To identify issues related to access to essential medicines and pharmaceutical policy within WTO Agreements and to inform the Member States;

(2) To study the implications of globalization on innovation, as well as development, production, marketing and medicine prices, aiming to identify potential impacts of the TRIPS Agreement and other trade agreements on acccess to essential medicines;

(3) To inform Member States about the necessity to adopt measures to protect public health.

The resolution provided WHO with the mandate to examine, through a public health lens, the new framework of the multilateral trade system after the establishment of the WTO (as stated in Chapter 4). Then, in 1997, the WTO launched its first publication on the TRIPS Agreement and Public Health — *Globalization and Access to Drugs* – which contained information to advise Member States how to implement the TRIPS Agreement in a way that maximizes benefits and minimizes negative impacts on access to medicines (Velasquez & Boulet, 1999).

This publication contains a brief history about international trade rules and provides guidance for policymakers from the health sector-who generally do not have a background in legislation of intellectual property rights-about the potential impact of the TRIPS Agreement on public health and access to medicines. Authors identified and described the flexibilities and safeguards of the TRIPS Agreement that could be implemented by Member States in order to protect public health as well as promoting access to medicines for their populations.

The publication was well received by representatives from developing countries and public interest non-governmental organizations involved in the international debate on access to medicines. However, it received bruising criticism from the Pharmaceutical Research and Manufacturers of America (PhRMA) and the United States government who argued that the publication was misleading and clearly biased. They stated that this document encouraged both piracy of patented medicines and inadequate protection of intellectual property rights in the pharmaceutical sector by WTO Members States (Velásquez, 2003).

Facing criticism, the WHO contracted an external group of specialists to revise the publication. In 1999, a new version containing a number of essentially editorial corrections was published, which corroborated the points of view and the interpretations made by the authors in the first edition.

In 1999, the 52nd WHA approved WHA Resolution 52.19 Revised Drug Strategy (RDS), which mandated the WHO to monitor trade agreements and their implications on public health, especially the WTO TRIPS Agreement. This resolution was approved after almost three years of controversial discussions. For example, during the 51st World Health Assembly in March 1998, the proposal (EB101.R24) had been rejected because it included questions related to trade

agreements and public health. Instead, the Assembly opted to send the proposal back to the Executive Board, which then formed an *ad hoc* working group to examine its most controversial points[11]

A lengthy process of discussion and consultation began, culminating with the development and approval of the WHA Resolution 52.19 at the 52nd World Health Assembly in 1999. The resolution emphasized that trade issues require examination from a public health perspective and also recognized that the TRIPS Agreement provides flexibilities and safeguards to protect health.

The resolution takes into account the concerns of many Member States, particularly developing countries, about the potential negative impacts of international trade agreements on local capacity, production and access to medicines. Therefore it is recommended that the Member States should: (1) ensure that public health interests will prevail over commercial interests, in the development and implementation of national drug policies; (2) explore and revise the flexibility and safeguard options in trade agreements, aiming to guarantee access to essential medicines.

This resolution requested the Director General to cooperate with Member States in monitoring and analyzing international trade agreements in order to develop policies and regulatory measures capable of maximizing the positive effects and mitigating the negative impacts of trade agreements (WHO, 1999).

One result was the creation of the WHO Network for Monitoring the Impact of the TRIPS Agreement and Globalization on Access to Medicines, composed of four WHO collaborating centers in pharmaceutical policy, clinical

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[11] The three most controversial points of the Resolution EB 101.R24 were:

"... (b) the new global agreements related to trade could have a negative impact on the capacity of local production and on access and price of medicines in developing countries.....[preamble].

1. Member States are urged:

. . . (2) to affirm that public health should prevail over commercial interests, in health and pharmaceutical policy...

2. To request to the Director General:

. . . (6) to cooperate with Member States in the analysis of agreements that were supervised by the World Trade Organization and their implications on public health and the pharmaceutical sector and to cooperate with the development of appropriate policies and regulatory measures." (PAHO, 1998).

pharmacology and health economics[12]. The Network's main objective is to develop, test and implement a methodology to monitor the impact of the TRIPS Agreement on access to medicines (WHO, 2001a). As part of this strategy, the following publications have already been released: Supakankunti *et al*. (2001), Bermudez *et al*. (2000a) e Oliveira *et al*. (2004).

Other important actors participating in the debate of trade agreements and public health are public interest NGOs, especially Doctors Without Borders (MSF), OXFAM, Health Action International (HAI), Consumer Project on Technology (Cptech) and Act Up.

In March of 1999, Cptech, HAI and MSF held a meeting to discuss the use of compulsory licensing as a strategy to expand access to ARV medicines (T'Hoen, 2002). In 2000, they organized a conference entitled, *The Amsterdam Conference on Increasing Access to Essential Drugs in a Globalized Economy*, which included the participation of 350 persons from 50 countries. During the conference, "The Amsterdam Statement" letter of commitment was drafted, whose directives provide guidance for NGOs and other actors involved in the TRIPS Agreement and Public Health debate (T'Hoen, 2002). Other NGOs, such as OXFAM (Cut the Cost campaign), the Treatment Action Campaign from South Africa (TAC) and Act Up entered into the discussion later.

The 1999 United Nations Development Program (UNDP) Report on Human Development addressed the issue of the TRIPS Agreement and access to medicines. This was the first time that the United Nations took a position on this subject. This report pointed out the potential downsides of the new intellectual property system for developing and least developed countries. For example, the proposed modifications to IPR legislation required by TRIPS can be so restrictive that they go against national interests. For developing countries, the costs of maintaining this type of patent system outweigh the benefits (T'Hoen, 2002).

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[12] WHO Collaborating Centers are responsible for the collection of data in their respective geographical regions: Department of Health Economics, Faculty of Economics from the University of Chulalongkorn – Thailand (Asia); National School of Public Health, Oswaldo Cruz Foundation-Brazil (Latin America and the Caribbean); London School of Economics – United Kingdom (Europe).

Then, the United Nations Sub-Commission on the Promotion and Protection of Human Rights published resolution 2000/7 on Intellectual Property and Human Rights (UN, 2000). This resolution declares that a conflict exists between the TRIPS Agreement and International Human Rights Law: "The implementation of the TRIPS Agreement does not adequately reflect the fundamental nature and indivisibility of all human rights, including the right of everyone to enjoy the benefits of scientific progress and its applications, the right to health, the right to food and the right to self-determination".

In 1999, during the 3rd WTO Ministerial Conference in Seattle, the Joint Program of the United Nations on HIV/AIDS (UNAIDS) highlighted the risks that policies and international trade agreements could have on access to goods and services essential for the prevention and treatment of HIV/AIDS. UNAIDS also supported: (1) differential pricing for HIV/AIDS related products — like condoms and pharmaceutical products; (2) reduction or elimination of customs tariffs for products related to the prevention or treatment of HIV/AIDS; (3) measures to promote generic drug competition and using the Bolar exception; and (4) using compulsory licensing.

In 2001, during the 54th World Health Assembly, Brazilian representatives criticized the methodology used in The World Health Report 2000 Health Systems: Improving Performance (Almeida *et al*, 2001; Noronha, 2001). Additionally, because Brazil was a part of the WHA Executive Board during 2001, they pushed the issue of national drug policies, which was not included in the WHA agenda, into the discussion "Strengthening Health Systems". After bitter clashes, the WHA Resolution 54.11-WHO Medicine Strategy was approved (WHO, 2001b). The impact of trade agreements on access to medicines is mentioned several times and the resolution reaffirms the WHA request that the WHO Director General should continue to analyze the impacts of trade agreements on health.

The resolution, in addition to previous WHO Revised Medicine Strategy resolutions, urged Member States to cooperate with respect to Resolution 2001/33 of the United Nations Commission on Human Rights. The latter recognizes that access to medicines in the context of pandemics such as HIV/AIDS, is a fundamental element to obtain the human right of enjoying the highest attainable level of physical and mental health.

In 2002, since the issue of national drug policies was included in the 55th World Health Assembly agenda, the Brazilian delegation presented a proposal for resolution, which received support from various other countries. After arduous discussions the proposal entitled, "Ensuring the Accessibility of Essential Medicines" was approved. This new Resolution mentioned the recently approved Doha Declaration on the TRIPS Agreement and Public Health, and also reaffirmed the previous year's resolution, which highlighted the need to examine the impact of international trade agreements on access to medicines. The Resolution also calls attention to the relationship between access to medicines and the recent changes in intellectual property legislation of Member States, in order to comply with the TRIPS Agreement (WHO, 2002).

The 56th World Health Assembly was held in May 2003, and one of the most polemic issues originated from a proposal formulated by the Brazilian Delegation, which also received the support from various developing countries. After one week of intense debates, Resolution WHA 56.27-Intellectual Property Rights, Innovation and Public Health- was approved by consensus (WHO, 2003). An important result of this resolution was the establishment of the Commission on Intellectual Property Rights, Innovation and Public Health (CIPIH). The Commission is composed of ten high level technical members who began activities in April 2004 (WHOa, 2004). The 57th World Health Assembly in May 2004 increased the Commission's mandates, and in 2006 they will present a final report.

The theme of intellectual property and access to medicines was discussed during the World Health Assembly in 2004 through Resolution WHA 57.14 Scaling up treatment and care within a coordinated and comprehensive response to HIV/AIDS (WHOb, 2004).

The TRIPS Agreement and the Doha Declaration: what are the interests at stake?

The first episode of clashes between pharmaceutical patent holders and government authorities, who are responsible for implementing access to medicines policies, occurred in 1998. After President Mandela signed the South African Medicines and Related Substances Control Amendment Act (Act. 90/1997), the Pharmaceutical Manufacturers' Association of South Africa together

with 39 transnational pharmaceutical industries filed a lawsuit against the Government of the Republic of South Africa in the High Court of Pretoria alleging that these changes violated the TRIPS Agreement and the South African Constitution. The litigation procedures resulted in an immediate suspension of the Amendment.

The Amendment Act was entirely consistent with the TRIPS Agreement provisions: it created a legal framework aiming to increase the availability of lower-cost medicines in the country. The main components of this Act that were questioned by the pharmaceutical companies were: (1) generic substitution for drugs with expired patents; (2) the establishment of a committee to regulate medicine prices transparently; (3) incorporation of the exhaustion of rights mechanism at the international level (parallel imports); and (4) establishment of an international competitive tendering system to assure provision of medicines for the country.

The litigation against South Africa included governments from other countries, such as the United States and the European Union, headquarters to the pharmaceutical company litigants. Together, they threatened to instate trade sanctions if South Africa did not revoke the Amendment, which damaged the commercial interests of their industries. Other actors were involved in this conflict, among those, representatives of the international campaign of access to medicines, particularly from the NGOs mentioned previously. NGOs played a decisive role in mobilizing public opinion against the United States, whose position centered upon defending the commercial interests of its companies without considering the impact on human rights. For example, due to pressure from NGOs during the United States Presidential campaign, the US government was forced to reverse its position against South Africa[13].

In April 2001, after three years of clashes and intense international pressure, the litigants were obliged to withdraw their lawsuit against South Africa. This happened for two reasons in particular: first, the litigants lacked technical arguments since the amendment did not violate the TRIPS Agreement in any

[13] In December 1999, after numerous protests, the United States government withdrew South Africa from the 301 Watch List, where countries that have violated trade rules are placed. (Benkimoun, 2002).

way and second, the pharmaceutical companies lost government support from the US and Europe. Harvey E. Bale, president of the International Federation of Pharmaceutical Manufacturers (IFPMA), stated that the pharmaceutical companies originally benefited from the support of the US and European governments. However, once the litigation process commenced, political support disappeared due to the general backlash that arose, which radically changed the original political context (Benkimoun, 2002). One of the principal arguments used by activists was that 400,000 people died of AIDS during the suspension of the amendment, because they could not afford to pay for treatment.

This episode was groundbreaking for the following reasons:

1. It contributed to the debate on the public health implications of the TRIPS Agreement in different international forums. This clash exposed the tensions that exist between the interests of patent holders and the right to life of millions of sick people;
2. It demonstrated the importance and necessity of international activism. NGOs organized rallies in the US and Europe, to stop their governments from supporting the litigating pharmaceutical companies. These actions caused the US government to reevaluate and change their policies on issues related to trade and public health;
3. The United Nations Organizations, particularly UNAIDS and the WHO, demonstrated their relevance as supranational mediators in conflicts of interest.

During the WTO 3rd Ministerial Conference in Seattle, which took place from November 30th through December 3rd in 1999, some WTO Members (European Union, Hungary, Japan, Korea, Switzerland and Turkey), proposed the exclusion of patentability for all medicines on the WHO Essential Medicines List, or, that developing countries could issue Compulsory Licenses for these medicines. It was hoped that this measure could provide an incentive for patent holders to license their products locally, under appropriate conditions, in order to make these drugs available at reasonable prices (WTO, 1999).

However, this proposal did not increase access to medicines in developing countries; on the contrary, it might limit the use of Compulsory Licensing to only a few patented products on the WHO Essential Medicines List.

At this time, only 11 of the 306 medicines on the list were patented (T'Hoen, 2002).

During the Seattle Ministerial Conference, President Clinton announced changes to United States policy on intellectual property rights and access to medicines. Due to the pressure from NGOs and international public opinion, the American government decided that the US Trade Representative (USTR) together with the Department of Health and Human Services, would establish new processes and guidelines to analyze questions related to health and Intellectual Property Rights.

In February of 2001, the United States took action against Brazil at the WTO Dispute Settlement Body, alleging that article 68 of the Brazilian Industrial Property Law (9279/96) violated the TRIPS Agreement. Article 68 establishes that the lack of local production of the patented product is ground to issue a compulsory license.

The United States argued that this paragraph of Brazilian law violated articles 27.1[14] and 28.I1 of the TRIPS Agreement. The Brazilian government defended itself arguing that its industrial property legislation does not interfere in any way with the provisions of the TRIPS Agreement. Article 68 had been formulated based on Article 5(2) of the 1967 Paris Convention, which states: each country of the Union can adopt legislative measures, such as compulsory licensing, to prevent abuses resulting from exercising exclusive rights conferred by the patent, which include the **lack of exploitation.**

There are contradictions implicit in the TRIPS Agreement and this has generated controversy amongst experts in the field of intellectual property rights (Correa, 1996; Barbosa, 1999). Article 27.1 prohibits any type of discrimination as to the place of invention, the field of technology and whether products are imported or locally produced. However article 2.1 allows Member States to abide by the clauses described in article 1 through 12 and 19 of the 1967 Paris Declaration.

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[14]Article 27.1 of the TRIPS Agreement establishes that: "... patents shall be available and patent rights enjoyable without discrimination as to the place of invention, the field of technology and whether products are imported or locally produced."

Why is the local exploitation of a patent important? According to Gontijo (2003), when a country grants exclusive rights to exploit an invention it has to receive something in return. From this perspective, there are two kinds of benefits: the first and most common is the disclosure of the invention. This allows a country to increase local knowledge and to reduce the time spent on research, as long as the invention is marketed only after patent expiration. The second benefit is local production.

It is important to mention that industrialized countries like the United States, England, France and Germany all required local exploitation of foreign patents in order to develop local production capacity, thereby increasing the capabilities of their manufacturing industries. Therefore, the greatest benefit a country can obtain from a foreign patent is its local production. If not, these inventions merely become instruments of the market, favoring importation, which leads to trade imbalances (Gontijo, 2003).

In June 2001, to de-escalate the tense situation between the United States and Brazil, Brazil agreed to sign a bilateral agreement with the US as long as the action against Brazil was withdrawn from the WTO Dispute Settlement Body. The US withdrew the action after intense international pressure from NGO activists, who argued that an unfavorable decision for Brazil could negatively impact the continuity of the National AIDS Program. This Program guarantees universal access to care for PLWHA (law 9.313/96) and is considered an example for other developing countries.

Another important step occurred in February 2001 when the European Union adopted the Action Programme to Accelerate the Fight Against HIV/AIDS, Tuberculosis and Malaria. This Program inspired debates and resolutions in the European Parliament to recognize potential problems between the TRIPS Agreement and access to medicines, as well as highlighting the need for a new equilibrium and redefinition of priorities (EU, 2001; T'Hoen, 2003). In June 2001, on the wave of a large global movement for access to medicines, New York was host to the United Nations Special Session on HIV/AIDS, which produced the Declaration of Commitment on HIV/AIDS (UN, 2001). Governments of 189 countries committed to implement integral programs composed of national and international actions to combat the HIV/AIDS epidemic, demonstrating that care, including access to medicines, support and prevention are indivisible

components for an effective response. The Declaration establishes a number of specific goals and targets that include:

(1) Reduction in transmission of the virus in children and adolescents;

(2) Improving HIV/AIDS education;

(3) Guaranteeing access to care including treatment;

(4) Improving support for orphans

The Declaration also mandated that the United Nations General Assembly dedicate at least one day each year to evaluate the progress and implementation of the established goals (UNAIDS, 2003).

To achieve the goal of guaranteeing access to care and treatment for PLWHA, the Declaration established article 55, that urges countries, "to cooperate constructively in strengthening pharmaceutical policies and practices, including those applicable to generic drugs and intellectual property regimes, in order further to promote innovation and the development of domestic industries consistent with international law."

In April 2001, a group of African countries, known as the African Group, brought up the need to include the access to medicines debate into the TRIPS Council agenda[15]. This request was based on the immense crisis of the HIV/AIDS epidemic on the African continent[16] and also due to pressure from transnational pharmaceutical companies and developed country governments.

In June, a Special Session of the TRIPS Council was held about intellectual property and access to medicines. This reunion was a milestone in the history of the multilateral trade agreement system because it marked a change in the

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[15] The TRIPS Council meets every three months to discuss different controversial and ambiguous issues related to the TRIPS Agreement. Separate Councils exist to discuss the other WTO agreements. What is discussed in these Councils is reported to the WTO Council General. These discussions become part of the agenda for the WTO Ministerial Meetings, which occur every two years.

[16] In December 2000, WHO and UNAIDS estimated a total of 36.1million people living with HIV/AIDS in the world (UNAIDS, 2001). Of these, more than 95% were living in developing countries in Africa, Latin America, Asia and Eastern Europe. The largest number of cases, 25.3 million (70%), occurred in sub-Saharan Africa. Not only do these statistics show the seriousness of the HIV/AIDS pandemic, but also the dramatic and radically unequal geographic and social distribution of the disease.

WTO paradigm, recognizing that intellectual property rights were neither absolute nor superior to other fundamental rights (Velásquez, 2003).

In the Special Session, Zimbabwe, on behalf of the African Group, formulated a proposal urging WTO Member States to issue a special declaration affirming that none of the TRIPS Agreement provisions should impede Member States from taking the necessary measures to protect public health.

In September, the TRIPS Council dedicated one full day to discuss access to medicines. The African Group, with the support of 19 other countries, presented a draft of the Ministerial Declaration on the TRIPS Agreement and Public Health. This draft reinforced the idea that the TRIPS Agreement should not limit the autonomy of Member States to formulate their own public health policy. Developed countries such as the United States, Japan, Switzerland, Australia and Canada prepared an alternative draft, emphasizing the importance of intellectual property protection for research and development. This draft intended to limit the use of TRIPS Agreement flexibilities to special situations of crisis or national emergency (T'Hoen, 2002).

In November, during the Fourth WTO Ministerial Conference in Doha, Qatar, the development of poor countries was discussed (WTO, 2002). An important result of this Conference was the Doha Declaration on the TRIPS and Public Health, which is considered a victory for developing and least developed countries, principally because it recognizes the countries' autonomy to implement the TRIPS Agreement in the best possible way for public health.

The Doha Declaration recognizes the gravity of the public health crises that affect the majority of developing countries, especially HIV/AIDS, tuberculosis and malaria, among others. The Declaration also reflects developing countries' concerns related to the TRIPS Agreement and public health.

The conditions that facilitated issuing the Declaration were: (1) the mobilization of developing countries, who acted together in a block; (2) the strong pressure from international NGOs and public opinion expressed in the media; (3) the fact that the United States and Canada had threatened to issue a compulsory license against the German company Bayer, the producer of ciprofloxacin, during the anthrax scare and its use in biological terrorism (T'Hoen, 2002).

The majority of developing countries and the generic pharmaceutical industry received the Declaration with enthusiasm. Since then, developing countries have achieved greater freedom to incorporate and utilize the TRIPS Agreement flexibilities to increase access to care for their populations. For the generic industry, the Declaration was an important advance because it reinforced each country's right to incorporate all TRIPS flexibilities, such as establishing the grounds to issue a compulsory license and freedom to use the Bolar exception.

This enthusiasm was not shared by the transnational pharmaceutical industry, which reacted to the Declaration with the following arguments:

(1) patents are not the principal barrier to access to medicines in poor countries — the lack of organized health care systems and national wealth are the principal barriers to access (Attaran & Gillespie-White, 2001);

(2) weakening patent protection could have a negative effect on research and development of new drugs Bale (2002).

(3) India, China and other developing countries were able to increase market share by selling copies of patented drugs to countries without technological capacity, who had issued compulsory licenses. Transnational pharmaceutical companies are concerned that the generic industries of these countries will prioritize their commercial interests above the necessity for innovation (Bale, 2002).

Regarding access to medicines, Velásquez *et al*. (chapter 4) stated that, "the Doha Declaration recognizes that medicines are not just another commodity and may be differentiated from other inventions in order to protect public health". Paragraph 4 of the Declaration reaffirms the principles expressed in article 8 of the TRIPS Agreement and emphasizes that access to medicines is an important component of health policy:

> " 4. We agree that the TRIPS Agreement does not and should not prevent members from taking measures to protect public health. Accordingly, while reiterating our commitment to the TRIPS Agreement, we affirm that the Agreement can and **should be interpreted and implemented in a manner supportive of WTO members' right to protect public health and, in particular, to**

> **promote access to medicines for all**. (bold text emphasis of the authors). In this connection, we reaffirm the right of WTO members to use, to the full, the provisions" in the TRIPS Agreement, which provide flexibility for this purpose.

Paragraph 5 establishes how certain rules and flexibilities of the TRIPS Agreement could be interpreted under the Declaration. For example, for developing countries, the compulsory licensing mechanism is an important instrument to achieve some health policy objectives, such as guaranteeing access to medicines for all by purchasing copies of patented medicines at lower prices (Correa, 2002). Sub-paragraph 5.b states that, "each Member has the right to grant compulsory licenses and the freedom to determine the grounds upon which such licenses are granted". This is important because the majority of developing and least developed countries are more vulnerable to pressures from the developed countries with whom they have entered into bilateral and regional trade agreements. These agreements intend to enforce more restrictive trade rules than those already established in TRIPS Agreement[17].

The question of issuing a compulsory license in countries without technological capacity for local production went without a solution for almost two years. Paragraph 6 of the Declaration mandated that the TRIPS Council would find an expedited solution by December 2002.

The lack of technological capacity for local production was a barrier to issue a compulsory license, because TRIPS Agreement article 31(f) establishes that production under a compulsory license should be destined to supply predominantly to the licensee's domestic market. Therefore, countries that could produce licensed medicine were not allowed to export to countries that did not have local manufacturing capacity.

This issue was discussed and negotiated in different forums, including various TRIPS Council meetings, for almost two years. A solution that fully satisfied all parties involved in the debate was extremely difficult to find (T'Hoen, 2002).

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[17] The second draft of the Free Trade Area of the Americas (FTAA) contained more restrictive provisions than the TRIPS Agreement. For this reason, any more restrictive trade agreement is referred to as TRIPS-plus.

What were the interests at stake? How was it possible to find a solution that, on the one hand, increased access to medicines, while on the other hand attended to the interests of the transnational pharmaceutical industry, including profits on investments in research and development? According to Pascal Lamy, the Trade Commissioner of the European Parliament (letter January 11, 2003), these concerns expressed by the transnational pharmaceutical industry were exaggerated because, "...if the poor countries are unable in any case to buy the medicines, where are the lost profits for the industry, where is the opportunity cost, where is the problem?" This means that the majority of countries without manufacturing capacity are so poor that they do not participate in the global pharmaceutical market, hence, they do not contribute to the generation of profits[18]. In conclusion, mechanisms that guarantee access to medicines for poor populations will not interfere or diminish the financial return of the pharmaceutical industry.

In order to preserve the interests of the transnational pharmaceutical industry, any mechanism to promote access must be transparent, including notification procedures and safeguards against diversion (re-exportation). The possibility of re-exportation exists for a medicine that is imported under compulsory licensing to countries where this drug is marketed at a higher price.

The solutions proposed for the paragraph 6 problem included: (1) the United States proposed a moratorium[19] for AIDS, tuberculosis and malaria and eventually a limited list of infectious diseases; (2) the European Union proposed, through the use of Amendment 196 (Directive 2001/83/EC), a "suspension" of article 31 (f) of the TRIPS Agreement, "in cases which the drug is exported to a third country, that has issued a compulsory license, or one in which it is not protected by patents"; and (3) the proposal from the Mexican Ambassador Eduardo Perez Motta[20].

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[18]According to IMS estimates for 2002, the pharmaceutical market generated 406 billion dollars, of which 80% come from the United States, Europe and Japan. The remaining 20% came from the other parts of the world home to 80% of the planet's population.

[19] The United States promised not to go to the WTO Dispute Settlement Body when a country without the technological capacity issues a compulsory licence for drugs used to treat AIDS, tuberculosis and malaria.

[20]For a detailed discussion of the legal mechanisms available for a solution to paragraph 6 of the Doha Declaration see Correa, 2002 and Abbot, 2002.

After three months of debates and negotiations, the TRIPS Council meeting was held in December 2002 in Tokyo. In this meeting the proposal developed by the Mexican Ambassador Eduardo Perez Motta -president of the TRIPS Council- was rejected. The proposal included the following components: (a) Definition of a Pharmaceutical Product; (b) Geographic Coverage (definition of countries eligible to import and export); (c) Transparency (notifying the TRIPS Council and putting all information about the process on the website); (d) Safeguards to prevent trade diversion (making the information public in regards to the amount of medicines necessary, special packaging as well as administrative and legal measures); (e) Legal Mechanisms (waiver of article 31 (f) of the TRIPS Agreement for the exporting country[21] and a waiver of article 31 (h) for the importing country; (f) transfer of technology and capacity building in the pharmaceutical sector (encouraging cooperation between exporting and importing countries); and (g) the decision would be in force until an amendment to article 31 of TRIPS resolves the problem of countries without technological capacity.

The majority of country representatives and interest groups present at the meeting harshly criticized Ambassador Perez Motta's proposal. A coalition of NGOs developed a document asking the delegates to reject Motta's proposal. They argued that the proposal: (1) ambiguously defines a pharmaceutical product (2) limits the use of compulsory licensing in the importing countries (3) creates excessive safeguards to prevent against diversion (re-importation) (4) requires both the importing and exporting countries to issue compulsory licenses (5) does not permit the use of one of the authorized interpretations of TRIPS article 30; and (6) does not consider the generic industry interests (CPTECH *et al.*, 2002). In addition, the United States, pressured by a strong transnational pharmaceutical industry lobby, vetoed Ambassador Perez Motta's text, alleging that the scope of diseases defined was too large (T'Hoen, 2003).

Aiming to re-open negotiations, in January 2003, Commissioner Pascal Lamy developed a proposal that increased the list of diseases[22] contained in the United States proposal and introduced the WHO as an intermediary consultant

[21] A Waiver is a legal mechanism that permits the suspension of legislation, or parts of it, or its effects, for a limited time.

(South Centre, 2003). However, the proposal did not include other important public health problems, such as infectious and non-infectious diseases prevalent in developing countries, for which patented medicines exist. It was argued that the lists were developed on the basis of commercial criteria rather than public health needs.

According to an analysis in the South Centre Bulletin no. 59 (2003), all proposals would create two different systems: (1) for countries with technological capacity, they would have the freedom to issue compulsory licenses at any given time and (2) for countries without technological capacity, they would be subject to additional, more restrictive conditions and lose the autonomy to define what is a public health problem.

On August 30th, 2003, the TRIPS Council published the Decision (IP/C/W/405) entitled, "Paragraph 6 implementation of the Doha Declaration on the TRIPS Agreement and Public Health" (WTO, 2003). This decision, launched on the eve of the 5th WTO Ministerial Conference in September in Cancun, Mexico, was identical to Ambassador Eduardo Perez Motta's proposal the year before. Chart 4 describes some important points of the Decision.

[22] The diseases covered under the Lamy proposal are the following: HIV/AIDS, malaria, tuberculosis, yellow fever, plague, cholera, meningococcal diseseas, African tripansomiasis, dengue, influenza, leishmaniasis, hepatitis, leptospirosis, pertussis, polio, shistosomiasis, typhoid fever, measels, dysentery and arboviruses.

CHART 4: Key points of Decision IP/C/W/405, August 30th, 2003.

	DEFINITION AND CHARACTERISTICS
PHARMACEUTICAL PRODUCT	Any patented product or product that was manufactured through a patented process in the pharmaceutical sector necessary to attend to public health problems. Also included are active ingredients for manufacturing as well as diagnostic kits necessary for product use
MEMBER COUNTRY IMPORTER	Any least developed Member country or any other country that has notified the TRIPS Council of its interest in using the system as an importer. The Member should notify the Council at any time if it will us the system in full or in a more limited manner. Some Members cannot utilize the system as importers and others can use it only in cases of national emergency or other circumstances of extreme urgency.
MEMBER COUNTRY EXPORTER	The country that utilizes the established system in the Decision to produce pharmaceutical products for export to designated importer Member countries.
LEGAL MECHANISM	*Waiver* of article 31 (f) of the TRIPS Agreement Article 31 (f) of the TRIPS Agreement establishes that the objective of production done under a compulsory license should be to predominantly supply the internal market. This article should be temporarily suspended so that the exporting country can produce drug for the importing country. When an exporting Member country issues a compulsory license unde the system established in this Decision, the patent holder should be adequately remunerated according to what is established in Article 31 (h) of the TRIPS Agreement. When a Compulsory License is issued fo the same products in the importing country, the obligation established in article 31 (h) should be suspended for these products because the exporting country already completed remuneration.
CONDITIONS FOR IMPLEMENTATION	The importing country should send a notification letter to the TRIPS Council with the following information: Name and quantity of the products needed; Proof that it is a Least Developed Country and that it does not have the capacity to produce the products in question; Confirmation that a Compulsory License will be or already was issued; The exporting country should issue a compulsory license that agrees to the following conditions: Only the quantity established by the importing country can be produced under this license; The products produced under this license should be clearly identified with specific labeling, to show that production was done through the decision s established mechanisms; The suppliers should distinguish these products from others through different packaging, colors and forms. Before sending the products to the importing country, the licensee should release the quantity and characteristics of the product that will be supplied on a website. Additionally, the exporting country should notify the TRIPS Council that a Compulsory License has been issued.
DIVERSION (RE-EXPORTATION)	To make sure that imported products under the system defined in this decision are used for public health, the importing country should take certain security measures. The measures taken should be proportional to the country's administrative capacity and to prevent re-exportation of the imported product.

International NGO representatives responded to the Decision with criticism and highlighted the following points, where were consistent with their position adopted the year before (FLECK, 2003):

1. The implementation procedures for compulsory licenses are slow, bureaucratic and increase administrative costs, which consequently increase drug prices;
2. Poor countries of Africa, Asia and Latin America have to go through unnecessary red tape to prove that they do not have manufacturing capacity;
3. The bureaucratic procedures dissuade generic drug producers, because they generate investment risks;
4. The requirement for different packaging can increase medicine production costs.

Despite the criticisms, the August 30th Decision may be considered a feasible solution at the present moment for countries without the technological capacity to produce the necessary medicines. However, the challenge remains to implement the Decision in a way that promotes access to medicines for populations in developing countries and least developed countries.

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Chapter 2

Bilateral trade agreements and access to essential drugs

Germán Velásquez

Thanks to bilateral trade agreements (or free-trade agreements - which go under the acronym FTA), Latin America may well export far more flowers, at the risk of finding itself without a single flower for the graves of those who will die from the lack of essential drugs. During the last three years, the developing countries have won one battle in the field of health, in the framework of the multilateral trade negotiations within the World Trade Organization (WTO). However, the bilateral trade agreements between the United States of America and Costa Rica, Central America, Morocco, Chile, Jordan, Singapore and Sri Lanka to name but a few, unfortunately seem to mark a step back. Not only do they undermine the progress made, they also seek to subject the health sector to a ruthless commercial rationale under which rights, values and principles are bartered just like textiles, computers or bananas. From the commercial angle, anything is negotiable, item for item. From the angle of public health, access to health care and to drugs are rights, and rights are not negotiated for merchandise.

The justification for "globalizing" drug patent standards, which is required by TRIPS, is that it represents a means of ensuring the continuity of research and development - R&D - into new products, which is largely in the hands of the private sector. According to this line of argument, research is highly expensive and the 20-year patent guarantees a monopoly, making it possible to recover and remunerate expenditure on research. In accordance with the WTO TRIPS Agreement, the Members of the Organization are required to provide a minimum of 20 years' protection for drug patents. This 20-year monopoly prevents manufacturers of generics from producing the drugs for this period, thus

preventing free competition, which in the last 50 years has significantly brought down the price of drugs. This system of research and development into new products, which is based on a commercial monopoly, keeps prices high and prevents most of the products developed from becoming immediately available to most of the people who need them.

It was four years before the developing countries discovered and achieved recognition for the exceptions for which the TRIPS Agreement makes provision in order to protect public health, and access to drugs in particular. At the November 2001 Ministerial Conference at Doha, these rights were ratified under pressure from the developing countries, who were united by the dramatic health situation caused by epidemics such as AIDS and many other diseases which may be prevented or cured with regular access to drugs. Over the last three years, the debate within the multilateral trade system has come to accept that the right to health ranks above commercial obligations. The discussion centred on the primacy of health and the possible exceptions that could be made. Tensions between health and trade appeared to abate; however, the requirements of the bilateral agreements -FTA- in respect of health-related intellectual property rights have now called into question a step forward which the international community had seemingly accepted and ratified. Many bilateral or regional trade agreements have sought to include measures relating to intellectual property that go beyond the requirements agreed upon in TRIPS: extension beyond 20 years of the validity of patent protection, restrictions on the possible use of exceptions such as so-called compulsory licences[1] or parallel imports[2] to protect health. As a rule, there is a tendency to restrict the rights acquired through multilateral negotiations within WTO by means of bilateral agreements in which bargaining power is dramatically unbalanced and unequal.

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[1] Compulsory licenses are authorizations that States may grant to third parties allowing them to use a patented drug without the consent of the patent holder in cases where a patent is not worked, health emergency or other circumstances which a country's legislation may define.
[2] Parallel imports, which are authorized by TRIPS in conformity with the principle of international exhaustion, are made when drugs protected by patent are imported, without the intervention or authorization of the patent holder, in order to benefit from the lowest prices at which the drugs have been legitimately sold in another country.

We shall now take a detailed look at the progress achieved, in what areas it has taken place and what has been won during the last three years, in order better to understand what is being lost or what we stand to lose.

For the first time in the fifty five years since the present international trade system -GATT and WTO- came into being, the November 2001 Ministerial Conference in Doha gave special treatment to medicines and adopted a declaration on the TRIPS Agreement and public health. It was recognized and affirmed that a medicine capable of preventing disease and death or restoring health is not simply another item of merchandise. The possibility of accepting that the debate on access to life-saving medicines is not a legal and commercial issue, but an issue of human rights and ethics was agreed upon. Some were so bold as to launch the idea that medicines are a global public good. As Carlos Correa has observed (Correa, 2002), the Doha Declaration represents, rather than the end of a process, the initial step for rethinking the TRIPS Agreement in light of the public interest; however, the FTA may dash the hopes raised by Doha.

The step taken at Doha is particularly important bearing in mind the contradictions that are appearing within the system of R&D for new pharmaceuticals; the purpose of patents is to enable research, but the fruit of the research is not available to all. Obviously, research and development of new drugs have to be preserved, as long as they are capable of saving lives as soon as they have been developed. During the last 20 years, hardly any research has been conducted to develop drugs for ailments such as Chagas' disease, leishmaniasis, schistosomiasis or sleeping sickness which affect millions of people in the developing countries.

The current drug R&D system offers no transparency as regards the actual cost of research, the way prices are set, how research priorities are determined or the attempts made to surround with a cloak of confidentiality the data in the health register, which should be in the public realm.

This latter issue - exclusive protection of data - merits special attention because, as Carlos Correa has stated, it may seriously undermine the flexibility authorized by TRIPS: the inclusion in FTA of the obligation, which is not required by TRIPS, to grant an exclusive period of protection for the test data submitted for marketing approval of pharmaceuticals. Article 39.3 of TRIPS prohibits solely the unfair commercial use of the confidential information submitted, whereas

the FTA would prevent a second applicant from availing itself of the approval granted to the party which submitted the information. Acceptance of this demand would signify that for five, eight or ten years, depending on the conditions accepted by each country, the national health authorities would be unable to base themselves on prior registration to approve a similar pharmaceutical. As Correa has noted, this will squeeze competitors' products out of the market, with inevitable consequences on drug prices.

The drug R&D system, which is founded uppon a commercial model whose basis is the monopoly afforded by patents, could find itself in a severe crisis in the next few years. The crisis would affect not only the developing countries, where the system is incapable of responding to current problems such as, for example, access to ARV, but also the developed countries. For this reason, suggestions are being made in some quarters for alternative and innovative mechanisms and solutions as a way out of what is a seemingly vicious circle. The challenge is to come up with global solutions that are sustainable in the long term.

Innovative solutions offering alternatives and ways of improving the current system are what are expected of the independent Commission on Intellectual Property Rights, Innovation and Public Health (CIPIH), recently established by WHO. The role of this Commission is inter alia to consider the importance and effectiveness of intellectual property regimes and other incentive and funding mechanisms in stimulating research and the creation of new medicines.

This is a particularly complex problem in which actors, interests and views of very diverse nature and origin interact; this calls for a comprehensive and multidisciplinary approach to the topic. The vision needs to reconcile existing international law and the various domestic legal regimes and to permit the operation of trade to be combined with respect for human rights.

The first requirement is to rationalize the system and to define priorities for research and development of new drugs on the basis of the actual health needs of people rather than of potential markets, as is the case today. Secondly, research should first and foremost be public and not private. How is public-sector research to be funded? There are a number of paths that should be explored a little further:

- part of the taxes raised on tobacco and alcohol, as is the case in Thailand;
- a tax on global sales of medicines;
- a tax on drug advertising, on which billions of dollars are currently spent or invested;
- a tax on drug wholesalers;
- a tax on gambling and lotteries;
- the Tobin tax on international financial transactions, as has been proposed by Canada, UNDP and Enrique Iglesias, President of IDB; 0.5% raised by means of an international agreement, the revenue from which would be used to finance research and development of new products which would immediately be marketed without patent protection and whose price would not include the cost of R&D, which would have already been covered by other means;
- medicines were afforded special status and treatment at Doha; why should special treatment not be reserved for R&D into new drugs?
- Shouldn't research in areas of interest to human life be considered a public good?
- Shouldn't governments meet the cost of clinical trials, which are extremely expensive and which at present have to be paid for by private industry, which incorporates the cost into research costs, thus passing it on to the price of the drug. Shouldn't clinical trials to develop new drugs be considered a public good? Isn't it true that there is growing distrust about manipulation of the results of trials by the pharmaceutical industry, which designs, conducts, supervises and pays for them? Just over one year ago, in a joint editorial, the editors of the world's main scientific journals expressed their concern about the manipulation of trials and of their results.

As W.K. Farlow of Oxford University has pointed out, whatever option, or combination of options is adopted, the new sources of funding will need to:

- generate large enough volumes of funds;
- be less costly and more efficient than previous sources of funding;
- guarantee stability over the medium and long terms.

It would be neither reasonable nor sensible to forcefully prolong, by means of a bilateral trade agreement, a system which is manifestly on the verge of a crisis. It is highly perilous to argue, in countries where mechanisms for redistributing national wealth are weak or non-existent, that so long as the trade balance is positive and exports increase three fold, then it matters little if the cost of medicines doubles. This also holds for countries where reimbursement of medicines has not yet fully become one of the services to which citizens are entitled. In 90% of the developing countries, medicines are paid for directly by patients, who are not reimbursed by some form of social security, as is the case in the industrialized countries. The unavailability of drugs may jeopardize the health systems which, with great difficulty, many countries have been building for a number of years.

According to a study carried out by Chaves (2004) from the Social Security Fund in Costa Rica, where 100% drug coverage has been achieved by means of State procurement of generic products, if it were impossible to purchase generics, coverage would extend only to 19% of the population. The same study showed that expenditure on ARV, which currently amounts to 5.9% of total expenditure on drugs, would rise to 15% if generics became unavailable.

However, not only the developing countries are affected. "For how long will it be possible for the health systems of the industrialized countries to bear the cost of reimbursing medicines, with the arrival, for example, of new drugs to treat cardiovascular diseases and cancer, or of the drugs that will be developed and patented, thanks to research carried out using public funds, into the human genome, and of the range of treatments connected with an ageing population?"(Velásquez, 2003)

In the United States of America, forecasts by the Medicare centres and Medicaid Services (CMS) show that national expenditure on health is set to double (from US$ 1 400 to 2 800 trillion) between 2001 and 2011 (Heffler *et al.,* 2002). According to CMS, expenditure on pharmaceuticals will increase three-fold between 2001 and 2011, rising from 142 to 414 billion dollars. The dilemma for private insurers will be whether to reduce coverage or to increase premiums.

In many European countries, expenditure on drugs as a proportion of health expenditure is significantly higher than in the United States, currently around 10%. By comparison it is 17% in France, 16.3% in Belgium, 17.1% in Greece and 12.8% in Germany. It is from the countries of Western Europe which,

despite the ultra liberalism of the Thatcher years, have managed to preserve access to health as a public right, that future solutions will come.

If the World Health Organization were called on to write a prescription for the FTA epidemic, what would it prescribe? The best remedy, as the Alma Ata Declaration recognized, is prevention. It could provide immunization against FTA in the form of a political decision which might read something like this:

"**Anything which might undermine the right of access to medicines and to health care IS NOT NEGOTIABLE and is to be excluded from any trade agreement".** To put it in words is easy; putting it into practice is another matter; everything will depend on the political courage, conviction and capacity of our present governments to avoid selling off access to health care for future generations in exchange for selling more flowers, whose cost will be measured in lives.

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Chapter 3

Ownership of knowledge-implications of the role of the private sector in pharmaceutical R&D

Carlos María Correa

Governments are responsible for a significant portion of global research and development (R&D) spending. However, since the 1980's, a steep decline in the share of government funds for R&D is a trend common to all major industrialized and many other OECD countries. While in the mid-1980s, an average of 45 percent of those countries' R&D funds were from government sources, by 1998 this figure had fallen to less than one-third. This trend does not reflect a reduction in total R&D expenditures, but a change in its composition: the private sector has a growing role in the creation of knowledge, including basic science[1]. In the largest OECD countries (with the exception of Italy), the private sector performed between 62 and 70 percent of total national R&D (National Science Board, 2002).

Private and public sources also coexist in pharmaceutical R&D. The division of labor in pharmaceutical R&D between the public and private sectors is related, at least in principle, to the nature of the knowledge that is fostered (Macroeconomic Commission, 2001). In most cases, the discovery of

[1] Though only about 1% of the industry's R&D budget is channelled into academic research, an increasing proportion (from 2,6% in 1981 to 6,4% in 1998) of such research is financed in OECD countries by industry (National Science Board, 2002). However, private industry invests the largest part of global funds for pharmaceutical R&D. Unlike the public sector, the industry's research agenda is dominated by profit making objectives. Most of industry's R&D concentrates on applied research and development, though funds are also devoted to basic research. In 1999, for instance, 24,5% of R&D spending was on basic research in UK, 36% in the USA and 18,4% in Canada (Patented Medicine Prices Review Board, 2002).

important new drugs is made by public institutions, which later license their development and exploitation to private firms. Some 70% of drugs with therapeutic gain were produced with government involvement (UNDP, 1999). Basic research that led to the discovery of potential "drug leads" has almost always been publicly funded at universities, in-house government facilities, or research institutes in Europe, North America, and Japan. Since the beginning of the 20th century, publicly funded research has led to major drug lead discoveries in, for example, tuberculosis, other infectious diseases and cancer. More recently, publicly funded research has led to the discovery of anti-retrovirals for the treatment of HIV/AIDS. Publicly funded genome research has also produced many drug leads (MSF, 2001). In the United States, the federally funded biomedical research supported by the National Institutes of Health (NIH) plays a vital role in new drug development, feeding into the R&D activities of the private pharmaceutical industry that operates under patent protection (Macroeconomic Comission, 2001).

In addition to this direct and important contribution, many developed countries' governments grant tax credits and other incentives for R&D [1]. Subsidies for pharmaceutical R&D are available in many developed countries, and are permissible, under certain conditions, under the WTO agreements. The US government, for instance, paid for the initial development, preclinical research, and clinical research of many important drugs, including many used for cancer and HIV-related diseases.

Given the objectives and nature of the industry's activities heavily rely on the acquisition and enforcement of patents worldwide. A common belief is that patents are normally acquired to protect new drugs, and thereby recover the substantial R&D investments made for increasing the range of available therapies. But the number of patents annually obtained to protect genuinely new pharmaceutical products is very small and declining, whereas thousands of patents are applied or granted for pharmaceutical-related inventions. Patents are growingly acquired in relation to "upstream" inventions, that is, scientific discoveries rather than specific technical solutions. This kind of patenting detracts from public domain knowledge that could be used downstream by many researchers to explore multiple inventive opportunities; it deprives society of the benefits that the widespread use and dissemination of basic scientific ideas could generate

(Macroeconomic Commission, 2001). The problems raised by this form of privatization of science have been addressed by an extensive literature (Barton, 2002; Eisenberg, 2001). Patents, on the other hand, are ordinarily acquired for a myriad of follow on, merely incremental or minor developments. This article examines the patterns of appropriation of innovation in pharmaceuticals, and how patents are often used as strategic tools to block or delay generic competition.

Innovation in pharmaceuticals

Today's technological advances in pharmaceuticals lay the basis for tomorrow's innovations, which in turn lay the basis for a next round, and so on. Developments are susceptible of further changes and improvements, by the original inventor or by others (Merges & Nelson, 1996). Innovation in this sector follows, hence, an essentially "cumulative" model of innovation[2].

Innovation in pharmaceuticals rely increasingly on the knowledge gleaned from preceding innovations and on generally available techniques (Long, 2000). Like in other sectors, innovation "has shifted away from models based on absolute novelty and first improvement towards a model in which innovation is no longer driven by technological breakthroughs but by the routine exploitation of existing technologies" (Foray, 1992).

Many of the new chemical entities of pharmaceutical use do not entail a genuine therapeutic progress; they are "me-too drugs" developed as a result of the great deal of emulation of successful drugs undertaken by rival companies" (Casadio Tarabusi & Vickery, 1998). Pharmaceutical innovation also includes a large number of improvements on or minor changes to existing drugs, and the identification of new uses of known products. Incremental innovation is often motivated by the objective of extending the commercial benefits derived from existing products, particularly when original patents expire and new patents may be used to prolong market exclusivity.

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[2] As opposed to the "discrete" model, where the prospects of variations and improvements of inventions are substantially bounded.

According to a Report of the National Institute for Health Care and Manegement (NIHCM), from 1989 to 2000, the FDA approved 1,035 New Drug Applications (NDAs). Of these, a third (35%) were products with new active ingredients, or NMEs. The other 65% used active ingredients that were already available in a marketed product. Over half (54%) were incrementally modified drugs (IMDs), or new versions of medicines whose active ingredients were already available in an approved product. The rest (11%) contained the same active ingredient as identical marketed products (NIHCM, 2002).

Priority NMEs, the most innovative type of new drugs, were rare in the 12-year period 1989–2000. Just 153 or 15% of all new drug approvals were medicines that used new active ingredients and provided significant clinical improvement. Drugs providing moderate innovation comprised another 28% of approvals. 57% of approvals were for drugs showing only modest innovation, at best. Of these, 46% made some modification to an older product containing the same active ingredient, while the remaining 11% were identical to marketed products. As a result, the NIHCM reports, priority NMEs contributed little to the increase in new products, and most growth came from products that did not provide significant clinical improvement, especially modified versions of older drugs (NIHCM, 2002).

Patenting cumulative innovations

The cumulative nature of innovation has important repercussions on the patent system. Though theoretically conceived to reward inventions marked by considerable originality, the patent system is plagued with grants covering incremental, minor, in some cases trivial, developments. They are not the product of inventive efforts, but rather the outcome of "taking a speedy path down a trail that was obvious to many" (Merges & Nelson, 1996:128). This kind of invention constitutes today the subject matter of the bulk of patents grants. In 2001, the United States Patent and Trademark Office granted over 171.000 patents, almost twice the number granted ten years before. This increase cannot be simply attributed to an increase in R&D productivity, but to the flexibility of the patent

system to permit the protection of follow on and other developments (Barton, 2000:1933-1934).

Moreover, there is increasing evidence about poor patent quality[3]. "Non-obviousness" or "inventive step" (one of the key patentability requirements) is assessed against a standard[4] that many follow on and routine innovations do not find difficult to meet. In addition, under patent law a claimed invention is presumed patentable, unless examiners can prove otherwise. "The procedures to evaluate patent applications", notes the US Federal Trade Commission (FTC), "seem inadequate to handle this burden[5]. The patent prosecution process involves only the applicant and the PTO. A patent examiner conducts searches of the relevant prior art...with only the applicant's submissions for assistance" (FTC, 2003). Such searches in most cases only include prior patents, and not books and journals. For this reason, the UK Royal Society has come up with the recommendation that "novelty searches should be broader, including the journal and trade literature as well as patents and patent applications" (The Royal Society, 2003). These problems are faced even in large patent offices, like the US Patent and Trademark Office (PTO), which operates with a staff of more than 6.000[6] and collects more than $ 1 billion in fees annually (GAO, 2002).

Large firms have rapidly learned how to exploit the pro-patent presumptions and the shortcomings in the examination process. They apply different strategies to offensively use patents as means to encumber or block potential competitors. Thus, "*blanketing*" strategies aim at turning an area into a

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[3] A poor-quality patent is one that is likely invalid or contains claims that are likely overly broad (FTC, 2003).

[4] Based on the fiction of what a "person with ordinary skill in the art" would have been able to derive from prior art.

[5] The rules applied in patent procedures tend to favor the issuance of a patent. According to testimonies collected by FTC, "if the examiner does not produce a *prima facie* case of obviousness, the applicant is under no obligation to submit evidence of nonobviousness." In addition, "office personnel must treat as true a statement of fact made by an applicant in relation to the asserted usefulness of the invention, unless counteravailing evidence can be provided that shows that one of ordinary skill in the art would have a legitimate basis to doubt the credibility of such a statement." Likewise, "there is a strong presumption that an adequate written description of the claimed invention is present when the application is filed." (FTC, 2003).

jungle or a minefield of patents, for example, "mining" or "bombing" every step in a manufacturing process with patents claiming minor modifications. "*Fencing*" refers a situation where a series of patents, ordered in some way, block certain lines or directions of R&D. "*Surrounding*" takes place "when an important central patent, especially a strategic patent, can be fenced in or surrounded by other patents, which are individually less important but collectively block the effective commercial use of the central patent, even after its expiration. Often, surrounding patents pertain to different applications of a basic invention (Granstrand, 1996)."*Flooding*" is based on the acquisition of many patents on minor on incremental variations on technology developed by another company (Sankaran, 2000).

Glasgow (2001) identifies five main ways that pharmaceutical firms employ to artificially extend the patent life of their drugs: (a) using legislative provisions and loopholes to apply for a patent extension; (b) suing generic manufacturers for patent infringement; (c) merging with direct competitors as patent rights expire in an effort to continue the monopoly[7]; (d) recombining drugs in slightly different ways to secure new patents and layering several patents on different aspects of the drug to secure perennial monopoly rights; and lastly, (e) using advertising and brand name development to increase the barrier to entry for generic drug manufacturers (Glasgow, 2001)

The application for and acquisition of patent rights over minor pharmaceutical developments is, thus, one of the strategies used to preserve and expand market dominance. Backed by substantial budgets for patent acquisition and litigation, pharmaceutical companies have been able to "evergreen" many of their most valuable patents, thereby substantially delaying the entry of generic competition. According to US lawmaker Waxman (one of the authors of the US Drug Price Competition and Patent Restoration Act pf

[6] Interestingly, US patent examiners are paid partly through bonuses for "disposal" of cases. While a granted patent is always a case of disposal, a rejection may not be, since the applicant may still amend the application and pursue its approval.

1984, commonly known as the "Waxman-Hatch Act") brand-name companies "have used creative lawyering to try and extend the period of their monopolies long past the intended time intended by Congress" (Seltzer, 2003)

The validity of pharmaceutical patents

Patenting certain features of a modified drug or process often enables pharmaceutical companies to extend intellectual property protection well beyond the term of the original patent. In fact, as noted by the NIHCM, "drug manufacturers patent a wide range of inventions connected with incremental modifications of their products, including minor features such as inert ingredients and the form, color, and scoring of tablets. In many cases, these patents discourage generic companies from trying to develop a competitive product" (NIHCM, 2002).

Poor quality patents acquired to encumber or delay generic competition are generally aggressively used against competitors. But they are likely to be invalidated totally or partially if subject to a more serious scrutiny than at the patent office. A US FTC study found that for nearly 75% of the drugs covered by the study, brand-name companies initiated patent infringement litigation against the first generic applicant[8]. A court decision had been made (at the time of conclusion of the study) for 53 drug products out of 75. A court decision resolved the patent infringement claims for 30 drug products. Generic applicants prevailed 73% of the time (FTC, 2002). Settlements were reached in 38% of the instances. Nine of these settlements obliged the brand-name company to pay a certain amount of money to the generic applicant. In seven cases the brand-name company licensed the generic applicant to use the patents for the brandname

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[7] For instance, Hoechst Marion Roussel (Aventis) paid Andrx several million US dollars to delay the introduction of a generic version of the drug Cardizem CD. The Federal Trade Commission settled a case in 2000 between Abbott Laboratories and Geneva Pharmaceuticals over charges of payments to delay the introduction of generic versions of patented drugs. Civil charges for anti-competitive practices have also been brought against Schering-Plough Corporation, Upsher-Smith Laboratories and American Home Products, on grounds that the companies entered into anti-competitive arrangements with the motive of delaying generic versions of a drug, K-Dur 20 potassium-chloride supplement (Sampath, 2003).

drug product prior to patent expiration, and in two cases the settlements allowed the generic applicant to market the brand-name drug product as a generic product, under the brandname company own marketing approval. In 18 instances, a court held that the brand-name company's patents were either invalid or not infringed (FTC, 2002:17-18). In addition, litigation took place against the second generic applicant in cases where the first generic applicant settled its patent infringement litigation. Out of a total of 20 drug products with first generic settlements, 9 drug products involved litigation with the second generic applicant. In 4 cases, there was also settlement with the second generic applicant, in 3 cases the second generic applicant won the patent infringement suit, while brand-name companies only prevailed in one infringement suit (FTC, 2002).

Illustration

There are many examples of evergreening strategies of pharmaceutical companies. Médicins Sans Frontieres (MSF), for instance, reports about the Glaxo Smith & Kline 1991 patent application to protect the combined use of AZT and 3TC. The patent application states that using the two drugs together has a surprising effect in that, e.g., the emergence of resistance is reduced. The patent granted by the European Patent Office was opposed by Novartis, who partially succeeded in reducing the scope of the patent .GSK then filed another patent application in 1995 to protect the broad idea of using AZT, 3TC and abacavir in combination, on the grounds that using the three drugs together has a surprising effect in that e.g. the emergence of resistance is reduced. GSK then filed a patent application in 1996 to protect the combination of AZT and 3TC in a tablet formulation (AZT, 3TC and a non-active ingredient, a glidant) (MSF, 2003).

Another telling example is paroxetine, an antidepressant compound. It has been known both in its basic form and in the form of its pharmaceutically acceptable salts since at least 1977. The patent makes explicit reference to the paroxetine base and to its maleate, and other pharmaceutically acceptable a acid

[8] The brand-name company generally sued all generic applicants if the drug product had annual sales larger than $500 million in the year the first generic applicant filed its marketing approval (FTC, 2002:18)

salts are covered by the reference in the general formula. It also refers to the use of a widespread general technique for preparing hydrochlorides. However, with 1985 priority, Beecham (who had obtained a license from the owner of the original patent) obtained patent EP 233.403 claiming crystalline paroxetine hydrochloride hemihydrate. Later, with 1995 priority, the company requested protection through application WO 96/24595 for four different forms of paroxetine hydrochloride anhydrate, and for various paroxetine hydrochloride solvates; with 1997 priority documents, it requested protection under WO 98/31365 for freeflowing paroxetine hydrochloride obtained using the "spray-dried" technique; with 1998 priority documentation, it applied (now as SmithKline Beecham), through WO 99/47519, a patent for a crystalline form of paroxetine free base, paroxetine free base in substantially pure form and paroxetine free base which is substantially solvent free; and with 1998 priority requested protection through WO 99/40084, for salts of paroxetine with various acids. In addition to endeavouring to protect every possible form of paroxetine base and of paroxetine salts with different acids in various forms, SmithKline applied for protection of the use of paroxetine in liquid form or as a solid absorbed in or by another solid (WO 99/26625 and WO 99/48499). Finally, the circle was rounded off by claiming paroxetine maleate, a product which had been described in the original patent US 4,007,196 (Correa, 2001; Hutchins, 2003).

Conclusions

Patents have become a key factor in the R&D process in pharmaceuticals. Though in certain contexts, they provide the incentives to develop new pharmaceutical products from which society may benefit, by its very nature they limit the diffusion of the innovations that they are intended to promote. When the innovation process is cumulative, strong protection for the first generation producer limits the scope of second generation producers, and slows down follow on innovation.

Patents often establish barriers to entry unjustified in terms of the technical contribution effectively made. Low standards of patentability have allowed a significant expansion of patent coverage. Strategic patenting diverts

resources into litigation and restrains legitimate competition. While this is taking place in both developed and developing countries alike, it is particularly worrying in the latter since competition laws are in many cases inexistent or poorly implemented, and domestic firms are generally too small to bear the costs and risks of litigation. Developing countries have struggled in the last years to confirm their rights to use the flexibilities allowed by the Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS), particularly in relation to parallel imports and compulsory licenses. Without abandoning these efforts, they should pay more attention to the way in which patents are examined and granted, in order to avoid abuses and the negative effects on access to medicines that secondary patents on non-inventive developments entail.

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Chapter 4

WHO in the Frontlines of the Access to Medicines Battle: The Debate on Intellectual Property Rights and Public Health

Germán Velásquez, Carlos M. Correa & Thirukumaran Balasubramaniam

Introduction

The Declaration on the TRIPS Agreement and Public Health (WTO, 2001), adopted by the World Trade Organization (WTO) Ministerial Conference in Doha in November 2001 marked a watershed in international law relating to public health. This landmark Declaration enshrines the principle that developing countries, the World Health Organization (WHO), civil society, international trade and legal experts, and the greater public health community have "publicly advocated and advanced over the last four years, namely, the reaffirmation of the right of WTO Members to make full use of the safeguard provisions of the TRIPS Agreement in order to protect public health and promote access to medicines" (WHO, 2002a). By singling out public health, and in particular pharmaceuticals, from other trade-related issues, the Doha Declaration recognizes that medicines are not just another commodity and may be differentiated from other inventions in order to protect public health.

The Declaration represented the culmination of a process initiated by the African Group in April 2001 at the WTO Council for TRIPS (TRIPS Council). Zimbabwe, on behalf of the African Group, requested a special session of the TRIPS Council with the objectives of clarifying the flexibility which Members were afforded under the Agreement and examining the relationship between the TRIPS Agreement and affordable access to medicines. This request arose from a growing sense of frustration among developing country Members of the WTO at the spate of pressures employed by the pharmaceutical industry and

certain developed country Members to impede developing country Members' application of the public health safeguards[1] of the TRIPS Agreement to ensure access to life-saving medicines. These disputes ranged from litigation and the threat of legal action in national courts to the initiation of dispute settlement proceedings under the WTO Dispute Settlement Understanding (DSU). The African Group observed that,

> a]s the recent upsurge of public feelings and even public outrage over AIDS medicines had shown, there was at the moment a crisis of public perception about the intellectual property system and about the role of the TRIPS Agreement, which was leading to a crisis of legitimacy for the TRIPS Agreement. Whilst this storm was raging outside the WTO, and legitimately so, Members inside the WTO could not shut their eyes and ears. Each Member, from developing and developed countries, had to respond, and had to respond adequately and appropriately. It was for this reason that the African Group was proposing the convening of a special session of the TRIPS Council to address the issues relating to TRIPS, patents and access to medicines.

This upsurge in public sentiment and awareness of the tensions between intellectual property rights (IPRs) and access to medicines was prompted by NGO and media scrutiny of the increasing difficulty of reconciling countries' obligations to abide by international trade agreements with public health needs. This disconnect was perhaps best crystallised by the South African court case which saw an attempt by the multinational pharmaceutical industry to forestall the Government of South Africa from instituting a range of public health sensitive

[1] The public health safeguards of the TRIPS Agreement provide Members recourse to mitigate potential negative impacts of the Agreement, most notably its impact on the price of medicines. The TRIPS safeguards include setting standards for patentability which reflect public health concerns, legislative provision for compulsory licensing, exceptions to exclusive rights and other measures which promote competition, full use of the transitional period and legislative provision for parallel importation (WHO, 2001).

measures including parallel importation,[2] compulsory licensing,[3] generic substitution and international price tendering. This court case and other similar actions, including the WTO dispute settlement case brought by the USA against Brazil on its local working provision on compulsory licensing, resonated with the international community because of their inextricable association with the HIV/AIDS pandemic.

In 2004, WHO estimates the number of people infected with HIV/AIDS to be between 34 and 46 million (WHO, 2004). Two thirds of the total live in Africa, and one fifth in Asia. A typical course of highly active antiretroviral therapy (HAART) recommended by the WHO for resource poor settings (WHO, 2002b) would have cost around $10 000 in 1998, the year the pharmaceutical industry initiated proceedings against the Government of South Africa. The South African court case and the US-Brazilian trade dispute highlighted growing concerns over the implications of the TRIPS Agreement for public health, in particular for access to medicines (Correa, 2002).

The special Session of the TRIPS Council on intellectual property and access to medicines, held in June 2001, was a landmark in the history of the multilateral trading system. The ultimate objective of the process initiated by the African Group and supported by like-minded WTO Members was to clarify and reach a common understanding that would resolve the uncertainty and ambiguity associated with the use of the TRIPS Agreement's public health safeguards. The

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[2] Parallel importation is importation, without the consent of the patent-holder, of a patented product marketed in another country either by the patent-holder or by another authorized party. Parallel importation enables promotion of competition for the patented product by allowing importation of patented products marketed at lower prices in other countries. If the importing country's patent regime provides that the patent-holder's right has been "exhausted" (in TRIPS terminology) when the patented product has been placed on the market in another country, the patent-holder cannot use his/her patent right in the importing country to prevent parallel importation. Article 6 of the TRIPS Agreement explicitly states that practices relating to parallel importation cannot be challenged under the WTO dispute settlement system.

[3] "Compulsory licensing enables a competent government authority to licence the use of an invention to a third party or government agency without the consent of the patent-holder. ... Grounds for compulsory licensing may include public interest, problems linked with national emergencies such as epidemics, public non-commercial use, or anti-competitive practices (Article 31). ... Any such use should be authorized predominantly for the supply of the domestic market of the Member authorizing such use (Article 31 f) (WHO, 2001).

emergent consensus, a testament to the collaborative work and efforts of actors which included developing countries, like-minded industrialized countries, civil society and intergovernmental organizations, posited that international trade rules should not undermine the legitimate right of WTO Members to formulate their own public health policies and adopt measures to safeguard public health. The Doha Declaration on the TRIPS Agreement and Public Health was based on the principle that public health interests are paramount in public health and pharmaceutical policies, a principle presaged in the Declaration's antecedent, the Revised Drug Strategy of the World Health Organization, as described below.

The Revised Drug Strategy and the "Red/Blue Book" controversy.

In 1996, the World Health Assembly, the WHO's highest governing body, passed a resolution on the Revised Drug Strategy requesting WHO "to report on the impact of the work of the WTO with respect to national drug policies and essential drugs and make recommendations for collaboration between WTO and WHO, as appropriate" (WHA, 1996a). This resolution provided WHO with the mandate to examine the new architecture of the multilateral trading system brought about by the establishment of the WTO in relation to public health. Proposals for this mandate were introduced by the Islamic Republic of Iran whose representative noted that his Government was very much concerned about the impact of the World Trade Organization on pharmaceutical industries in developing countries in the light of his country's efforts to promote and implement the essential drugs concept (WHA, 1996b). Although concerns over the inclusion of intellectual property into the multilateral trading system had been voiced by many developing countries during the Uruguay Round negotiations, this resolution marked the first time these concerns were broached in the international public health agenda.

Pursuant to the mandate of the World Health Assembly, the WHO Action Programme on Essential Drugs published a monograph entitled, *Mondialisation et Acces Aux Medicaments: les Implications de L'Accord ADPIC/OMC* (Velásquez & Boulet, 1998). This guide was written with the objective of informing health policy professionals with limited or no legal background on the potential impact of the TRIPS Agreement on public health and pharmaceutical policy. The authors

noted that, prior to the TRIPS Agreement, countries had considerable freedom to determine the standard of intellectual property appropriate to their local context. The TRIPS Agreement established minimum standards for the protection and enforcement of IPRs. The authors observed that the agenda of the Uruguay Round that preceded the establishment of the WTO was driven by the industrial policy objectives of developed countries with developing countries playing a minor role in the negotiations. Although the authors noted that TRIPS imposed standards historically derived from industrialized countries, the Agreement still provided considerable discretion to safeguard public health. As the monograph examined TRIPS from a public health perspective, the authors identified the safeguard provisions in the Agreement that enabled countries to protect health and promote access to medicines. These safeguards include compulsory licensing, parallel importation, limited exceptions to patent rights and the use of the transitional periods. They are built into the TRIPS Agreement to promote competition, ensure against the abuse of economic power and remedy anti-competitive practices.

This monograph, nicknamed the "Red book" because of its red cover, advocated interpretations fully within the ambit of the TRIPS Agreement and widely accepted by the academic literature. However, its publication provoked a heated response among certain quarters. While this document was well received by many developing countries, Ministers of Health from the non-aligned movement, and civil society, the pharmaceutical industry and some industrialized country Member States criticized the report as unbalanced and misleading. In the opinion of the Pharmaceutical Research and Manufacturers of America (PhRMA), this monograph was

> a deeply flawed document that misleads the public and creates a false impression of how the WTO TRIPS agreement[sic] will affect pharmaceuticals. The paper seeks to rationalize the continued piracy of pharmaceuticals inventions...and encourages WHO members not to implement adequate and effective intellectual property protection for pharmaceuticals (Bomballes, 1998)

The Government of the United States of America prepared a 17-page paper "pointing out the inaccuracies and false implications with which the document is riddled" (U.S. Government, 1998). WHO revised a revision of the

monograph with independent external reviewers and input from the WTO. A revised version, the "Blue book" was published in January 1999 with a number of essentially editorial corrections, confirming the views and interpretations given in the Red book.

At the same time, there was also controversy surrounding the revision of the World Health Assembly Resolution on the Revised Drug Strategy which would strengthen WHO's mandate to monitor international trade agreements. In January 1998, the Executive Board of WHO passed a draft resolution (WHO, 1998a) on the Revised Drug Strategy which urged Members States to

> "ensure that public health rather than commercial interests have primacy in pharmaceutical and health policies and to review their options under the Agreement on Trade Related Aspects of Intellectual Property Rights to safeguard access to essential drugs".

The draft resolution requested the WHO Director-General to

> "assist Member States to analyse the pharmaceutical and public health implications of agreements overseen by the World Trade Organization and to develop appropriate policies and regulatory measures".

This draft resolution was prompted by concerns of Board Members, including Canada, Egypt and Zimbabwe, on the potential impact of WTO agreements on access to medicines (WHO, 1998b). The representative from the Government of Canada noted that

> "experience had shown that those in the health sector needed to play a much more active part, both individually and collectively, in international trade discussions. Regrettably, industrial or intellectual property considerations often took precedence over health concerns in current trade negotiations. Moreover, the complexity of such discussions often made it more difficult to argue the health case. Much better international data on prices were needed, and he would urge WHO to collaborate with OECD, which had a significant effort under way in that connection" (WHO, 1998b).

In May 1998, this resolution was submitted to the Fifty-first World Health Assembly for consideration. It met with considerable opposition from a few WHO Members States. Furthermore, some countries opposed the operative paragraph instructing WHO to examine the TRIPS Agreement because it held that WHO was not the competent authority to interpret trade agreements. In order to reconcile the differences a drafting group was set up but, after over 15 hours of contentious negotiations, no consensus was reached. The resolution was reluctantly referred back to the Executive Board for further consideration (United States Mission to Internatrional Organizations – Geneva, 1998; WHA, 1998). An ad hoc working group comprising 59 Member States met from 12 to 16 October 1998 and drafted a compromise text. This resolution was subsequently approved by the 103rd Executive Board and the Fifty-second World Health Assembly. The new Revised Drug Strategy urged Member States to "ensure that public health interests are paramount in pharmaceutical and health polices" and requested WHO

> "to cooperate with Member States, at their request, and with international organizations in monitoring and analysing the pharmaceutical and public health implications of relevant international agreements, including trade agreements, so that Member States can effectively assess and subsequently develop pharmaceutical and health policies and regulatory measures that... maximize the positive and mitigate the negative impact of those agreements"(WHA, 1998).

The resolution provided WHO with a broad mandate, not limited to just the TRIPS Agreement, to analyse the implications of globalization on public health and to advise Member States, at their request, on public health issues in relation to international trade agreements. As noted by Ian Roberts, Special Adviser to South Africa's Minister of Health, the "importance of this resolution is that health now has a role in all international trade and finance agreements."(HAI/MSF, 1999)

South Africa: The intersection of public health and intellectual property rights

In 1996, South Africa introduced a National Drug Policy (NDP) to remedy structural deficiencies in its pharmaceutical sector inherited from the apartheid regime. Although South Africa boasted a sound domestic pharmaceutical industry, its health care system was characterized by the juxtaposition of a private health care system on par with the first world and a public health sector beset by third world conditions. This inequity in health care was compounded by the chronic inaccessibility of essential medicines in the public health sector. For example, in 1990 the private health care sector, which covered around 20% of South Africa's population, accounted for 80% of the country's total expenditures in pharmaceuticals (Department of Health, 1996). Furthermore, the growing HIV/AIDS epidemic highlighted the impact of prices of medicines in South Africa, among the highest in the world. Thus, the objectives of the NDP were to ensure an adequate and reliable supply of safe, effective drugs of acceptable quality to all citizens of South Africa and the rational use of drugs by prescribers, dispensers and consumers (Department of Health, 1996). In order to implement these objectives, the South African Drug Action Programme (SADAP) was established with funding by the UK Department for International Development (DFID) and executed with the support of the WHO Department of Essential Drugs and Medicines Policy (EDM).

The key objectives of the South African NDP were codified into law when President Nelson Mandela signed the South African Medicines and Related Substances Control Amendment Act (Medicines Act) in December 1997. The Medicines Act provided the Government of South Africa recourse to generic substitution, quality control of imported medicines, international competitive tendering for the public sector, an essential drugs list and standard treatment guidelines. Many of these measures were long-standing public health principles advocated by WHO. In addition to these measures, South Africa's Medicines Act adopted a regime of international exhaustion thus permitting the parallel importation of medicines.

Following the passage of the Medicines Act in December 1997, the research-based pharmaceutical industry and some industrialized countries worked in tandem to "repeal, suspend, or terminate" certain provisions of the Medicines

Act. In particular, they asserted that the parallel importation and generic substitution clauses of the Medicines Act contravened the TRIPS Agreement. In February 1998, the Pharmaceutical Manufacturers' Association of South Africa (PMA) and 39 other applicants filed suit against the Government of the Republic of South Africa in the High Court of South Africa alleging that the Medicines Act violated the South African Constitution. Although the PMA specifically targeted Section 15(C) of the Medicines Act, the subsequent litigation forestalled the entire Act thus freezing all the public health policy measures articulated in the NDP.

The Medicines Act conflict was singled out in the 1999 USTR Special Review. The entry for South Africa noted that the

> "Medicines Act appears to grant the Health Minister ill defined authority to issue compulsory licenses, authorize parallel imports, and potentially otherwise abrogate patent rights...During the past year, South African representatives have led a faction of nation's in the World Health Organization (WHO) in calling for a reduction in the level of protection provided for pharmaceuticals in TRIPS."(USTR, 1999)

The reference to WHO indicated the USG's displeasure at South Africa's leading role in the controversy over the Revised Drug Strategy during the Fifty-first World Health Assembly. With respect to South Africa's interventions at the World Health Assembly, PhRMA expressed concern that other countries would follow South Africa's path in implementing the public health safeguards of the TRIPS Agreement to the perceived detriment of holders of intellectual property rights. Although sub-Saharan Africa accounted for only 1% of the world pharmaceutical market (IMS Health, 1997), the implementation of the Medicines Act would set a precedent that the pharmaceutical industry and industrialized countries were loath to accept. In February 1999, the United States Department of State (State Department) reported to the US Congress on the US Government's efforts to repeal the South African Medicines Act:

> "All relevant agencies of the U.S. Government...have been engaged in an assiduous, concerted campaign to persuade the Government of South Africa (SAG) to withdraw or modify the provisions of Article 15(C) that we believe are inconsistent with South Africa s obligations and commitments under the WTO Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS)."(Department of State, 1999)

Despite the onslaught of over three years of trade pressures and sanctions, the Government of South Africa held its ground and refused to compromise its position on the Medicines Act. South Africa's position was strengthened by a range of different actors united in the principle that commercial interests should be subordinate to public health interests. This loose coalition of developing countries and certain segments of industrialized country governments, civil society, international organizations including UNAIDS, UNICEF, and WHO, international trade experts, and the greater public health community, was due to the international outcry raised by this diverse set of actors over the morally untenable position of the pharmaceutical industry and certain developed countries in the South African case. In May 2000, President Bill Clinton issued an Executive Order exempting sub-Saharan Africa from the US pressures to forestall their use of the TRIPS public health safeguards to mitigate the impact of the HIV/AIDS pandemic.

The role of the civil society coalition, which included ACT UP, Consumer Project on Technology, Health Action International, Health Gap, Médicins Sans Frontières, Oxfam, and the Treatment Action Campaign to name but a few, should not be underestimated ('t Hoen, 2002). Much of the progress of the access to medicines campaign can be credited to civil society efforts. In particular, civil society drew media attention to the South African court case and the greater question of IPRs versus public health. Using an array of tactics, which included protests, direct action, technical briefing seminars on TRIPS public health safeguards, and media coverage, civil society effected a major shift in OECD government positions vis-à-vis TRIPS and public health. Although the real motivations for the policy changes are not clear, the loss of the US and EU government support for the case, resulted in the withdrawal of the lawsuit by the PMA and pharmaceutical firms ('t Hoen, 2002). The victory of the South African Government marked a turning point in the TRIPS and public health debate and set a precedent for developing countries. South Africa's resolute defence of its National Drug Policy prevailed over the industrial might of certain OECD governments and the pharmaceutical industry because it was based on sound public health principles, it was TRIPS consistent and was based on WHO guidelines for National Drug Policies. This not only lent it moral legitimacy in the court of public opinion but also juridical legitimacy in the court of law.

The World Health Organization: Implementing the mandate of the Revised Drug Strategy

At the core of the Revised Drug Strategy resolution of the Fifty-second World Health Assembly was the principle that public health interests are paramount when formulating pharmaceutical and public health policies. In order to fulfil the mandate given to WHO to monitor the impact of globalization and international trade agreements on access to medicines, WHO established a Network for Monitoring the Impact of TRIPS and Globalization on Access to Medicines. This network is comprised of four WHO collaborating centres in Brazil, Spain, Thailand, and the United Kingdom and legal and public health experts with specialized knowledge and understanding of the public health and pharmaceutical dimensions of international trade agreements. The network has endeavoured to answer four main questions: (1) the effect of patent protection on the price of essential medicines, (2) the impact of patent protection on generic entry, (3) the impact of IPRs in spurring new drugs for neglected diseases and (4) the effect of TRIPS on transfer of technology and direct foreign investment. The Revised Drug Strategy and its successor, the WHO Medicines Strategy, instructed WHO to cooperate with Member States, at their request, to develop pharmaceutical and health policies related to international trade agreements. With respect to the TRIPS Agreement, WHO advised several Member States[4] on how to implement public health safeguards consistent with the Agreement.

Since the passage of the Revised Drug Strategy, WHO has provided technical guidance to Member States on the public health implications of the TRIPS Agreement and other international trade agreements through policy documents and regional workshops. Under the aegis of the Revised Drug Strategy, WHO briefed health, patent office and trade officials in over 60 countries on TRIPS implementation. WHO published and funded various papers, reports and monographs providing policy guidance to countries on public health and IPRs in relation to TRIPS safeguards, traditional knowledge, protection of test data, model

[4] Since 1996, WHO's work in this area has involved direct country support in Brazil, Brunei Darussalam, China, Dominican Republic, Indonesia, the Islamic Republic of Iran, Kenya, the Republic of South Africa, the Kingdom of Cambodia, Nicaragua and Thailand. This technical cooperation has involved assessing the patent status of antiretrovirals, analysing the IPR and drug regulatory provisions.

legislation, patenting strategies in pharmaceuticals, and co-authored a joint study with the WTO on the health and trade implications of the WTO Agreements. The crux of WHO's policy guidance with respect to the TRIPS and access debate has been guided by the core principles that the "enjoyment of the highest attainable standard of health" is a fundamental human right and that essential medicines are not just another commodity. Although WHO acknowledged the important role of IPRs in stimulating research and development of new drugs, it noted with concern questions raised about the impact of IPRs on the price of certain life-saving medicines and the failure of the IPR regime to stimulate the development of drugs for neglected diseases. In its policy guidance to Member States, WHO advocated the full use of the TRIPS public health safeguards, as appropriate, to protect public health and promote access to essential medicines. These safeguards included setting standards for patentability which reflected public health concerns, legislative provision for compulsory licensing, authorizing parallel importation of health care inventions, other measures which promote generic competition, the full use of the transition period accorded to least-developed countries under the Doha Declaration, and resisting pressures to adopt "TRIPS-plus" standards of IPR protection.

The road to Doha

The conflicts arising between safeguarding access to medicines and upholding obligations to international trade agreements brought two important issues to the fore on the debate on health and trade questions. The first was the realization that a combination of generic competition, advocacy and legislative provision of TRIPS safeguards had a significant pro-competitive effect on the price of medicines, as evidenced in the dramatic more than 95% price reduction in the indicative annual cost for a triple therapy antiretroviral regime from $10 000 in 1996 to $140 in South Africa in 2003. This realization was further confirmed when Brazil's negotiation after the threat to issue a compulsory licence on Merck and Hoffman-La Roche's antiretroviral patents resulted in a significant price reduction of antiretrovirals supplied to the Government of Brazil. The expediency with which Canada and the USA successfully threatened the use of the compulsory licensing to secure lower prices for ciprofloxacin following the anthrax scare after the events of 11 September 2001, confirmed the possibility of using TRIPS safeguards to promote access to essential medicines.

The second issue raised by the health and trade debate was the pressing need to ascertain the level of flexibility which WTO Members were afforded under the TRIPS Agreement. As the South African court case and the Brazil-US dispute over compulsory licensing showed, legal uncertainty created a "chill effect" on Members' efforts to enact and use the public health safeguards of the TRIPS Agreement. The African Group's request to hold a special session of the TRIPS Council to discuss intellectual property and public health related questions was accepted by WTO Members. Pascal Lamy, the European Union Trade Commissioner remarked,

> L'essentiel de notre position réside en un point clé : nous pensons que l'Accord laisse aux Membres de l'OMC une latitude suffisante pour mettre en place un régime de propriété intellectuelle susceptible de répondre aux préoccupations en matière de santé publique. Notre conviction est qu'il appartient aux Membres de l'OMC, au sein du Conseil ADPIC, d'interpréter cette flexibilité, plutôt que laisser cette tâche aux panels.(Lamy, 2001)

The adoption of the Doha Declaration underscored the principle that international trade rules could not and should not undermine the legitimate right of countries to protect public health. The Declaration, a validation of public health ideals anticipated by the debates on the WHO Revised Drug Strategy, was possible due to the resolute defence of these ideals by developing countries and their allies in civil society. The Declaration represents but a first step in making the multilateral trading system compatible with health interests. Much more needs to be done. The recently published report of the UK Commission on Intellectual Property Rights,[5] recognized the concerns articulated by developing countries, civil society and WHO that "one size fits all" intellectual property

[5] The United Kingdom Secretary of State for International Development, Clare Short, established the UK Commission on Intellectual Property Rights (CIPR) in May 2001 to consider how IPRs "could best be designed to benefit developing countries." (Forward to CIPR report by Sir Hugh Laddie, UK High Court Patents Judge). The six member panel brought different perspectives to the table, incorporating voices from developing and developed countries, with experience from fields including: economics, ethics, law and science and from academia, industry and government. See e.g. http://www.iprcommission.org/graphic/home.htm.

regimes, historically derived from those adopted in industrialized countries, are not appropriate for developing countries in different stages of economic development. Furthermore, the report concludes that developing countries should integrate their development policies, including on public health, into IPRs regimes suited to their conditions and needs.

It is now realised that the right to health and the expansion of trade are different issues. Essential drugs must be considered a global public good. Promoting the right to health involves guaranteeing the right to benefit from technological advances, and a recognition of the supreme value of human dignity, principles recognized in many international treaties and accepted by most states.

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Chapter 5

Effects of the TRIPS Agreement on the Access to Medicines: Considerations for Monitoring Drug Prices

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The concept of access in health encompasses some distinct, although correlated, dimensions, which address the compatibility between the patient and the health care system: availability, accessibility, accommodation, affordability and acceptability (Perchansky & Thomas, 1981; Luiza, 2003). When considering access to drugs in the context of the most frequent arguments over intellectual property (IP) protection, patents are predicted to have effects on three of these dimensions. For example, in the case of availability, innovation could be stimulated and better therapeutic options might become available to the public; for acceptability, the new drugs developed might be perceived by users as better therapies (whether or not they might actually be); and effects might also be seen on affordability, due to an increase of drug prices, pushed by the premium prices of patented products set by enterprises during the market exclusivity period, in order to recover research and development (R&D) expenses.

Much concern has been raised about the consequences of new, patented medicines to the health systems in developing and least-developed countries as they may represent an unbearable burden of treatment costs, hence hindering access to newer and better therapies. Nevertheless, it is not an easy task to infer the effect of IP protection on drug prices, and for such a purpose, one should consider the interplay of a myriad of factors that may have a role in drug pricing. Features that shape the supply and demand sides of the pharmaceutical market, along with background issues, and their connections must be understood in order to model the conduct of pharmaceutical companies in setting prices for their products.

Here, some of these features will be discussed, bearing in mind their relevance to drug pricing and focusing on access to medicines: innovation in the pharmaceutical industry, and the role of patents; market segmentation and competition, characteristics of the demand for pharmaceuticals; and regulation and health system organization. Finally, mapping the changes that can be expected from enacting the Trade Related Aspects of Intellectual Property Rights (TRIPS) Agreement through national legislation will guide the identification of what can be done to monitor the effect of drug patents on access to drugs in developing and least-developed countries.

Intellectual property and medicines: what do patents really mean?

Patents are generally regarded as the most effective mean of appropriating the benefits from innovation in the pharmaceutical industry. This occurs because of the very nature of the technology developed: a medicine is a molecular entity[1] plus the information about its effects in human beings – including therapeutic efficacy and safety. Hence, most of the investiment in new drug R&D is incurred to generate information, from preclinical stages to the phase III clinical trials required for granting product approval, which become available to the public (Scherer, 1996:360). As organic chemical synthetic and pharmaceutical formulation methods are reasonably available, an imitator can, in the absence of patents or other kind of market exclusivity, spend just a fraction of innovator investiment and consume much less time in developing a copy of the original product. The same is not true for a new producer that tries to "invent around", e.g. making slight modifications in the chemical structure of the drug that are not covered by the original patent granted, as this new product will also have to pass through all the clinical development phases. This is why pharmaceutical patents are considered incentives for innovation in this field: the gains derived from R&D spending, through charging prices well above the marginal production costs, will not accrue to imitators, at least during the exclusivity period.

[1] This is also true for herbal medicines if one considers them an assembly of molecules exerting a therapeutic effect.

However, profiting from innovation also depends on other features like complementary capabilities and assets required for the successful commercialization of an innovation (e.g. distribution channels, services, complementary technologies). These features guide strategic marketing decisions of firms which can choose to license their technology, to contract out, to integrate with others, or to invest in accessing such assets (Teece, 1986)[2].

As shall be discussed further, some of these capabilities and assets are correlated to factors that determine product price. Consequently, they should be considered when addressing the profitability of innovation in the pharmaceutical industry. Marketing strategies, for example, are aimed at reinforcing the attributes of new medicines, leading to favourable evaluations by consumers (patients and doctors) and, as a result, to an enhanced ability of determining drug prices.

Additionally, revenues generated by patented medicines are greatly skewed. Scherer (1993) estimates that about 55% of industry profits come from around ten percent of the drugs. Grabowisk and Vernon (2000) have studied two cohorts of new molecular entities (NME) launched from 1980 to 1984 and from 1988 to 1992, respectively, demonstrating that only 30% of products with greater revenues yielded values higher than the estimated average R&D investiment of US$ 231 million per new drug (DiMasi *et al.*, 1991). Despite the controversy on the validity of this last value[3], these figures indicate the inherent risk of this kind of investiment, but mainly reflect the different opportunities for profiting from innovation due to factors that drive the diffusion and the pricing of pharmaceutical products.

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[2] Consider, for example, the collection of small and medium size firms in the American biotechnology industry that rely on patent protection to create a strong bargaining position for a joint venture or a license deal with a large pharmaceutical enterprise that has production and market capabilities (Mazzoleni & Nelson, 1998).

[3] Refer to the work "Rx R&D Myths: The Case Against The Drug Industry

's R&D 'Scare Card'" (Public Citizen, 2001) for an accurate questioning on the original estimates made for DiMasi *et al.* (1991).

Patterns of Innovation in the Pharmaceutical Industry and Medicine Prices

Initially, one can consider the relationship between the innovative profile of new pharmaceutical products and their prices. Highly innovative medicines, whose formulation generally includs drugs that act by new pharmacological mechanisms of action, and which are often the first products in a market segment, are launched at premium prices. This is due to the less elastic demand generated by their therapeutic potential (*i.e.* consumers are more willing to pay for a product that supposedly offers a better health result) and the conditions of market competition. These products often become "blockbusters", and account for a great part of a firm's revenues. Their active compounds become the leads[4] for the development of new drugs with the same mechanism of action.

Lesser innovative products, the so-called *me too drugs*, composed of new molecules that follow a molecular structural pattern already established in a therapeutic group, tend to be launched on the market at similar or lower prices than previous competitors except when they show significant clinical advantages , like fewer side effects or a more convenient dosage regimen. In a recent study on pricing trends of new prescription drugs on the American market from 1995 to 1999, DiMasi (2000) analyzes the introduction of new products in specific therapeutic groups and describes the link between prices and degree of innovation.

In order to complete the picture, one should refer to the new products that do not contain new active principles, but rather consist of new formulations (including new dosage forms, like extended drug release), new combinations of molecules already on the market, or new salts or esters. Usually, these products have a lesser innovative profile when compared with previous ones – and hence, lower launch prices. Nevertheless, there may be exceptions, since some products can exert considerable therapeutic advantages, such as the antiretroviral drug combining lamivudine and zidovudine.

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[4] Strictly, the term *lead compound* is applied to the molecule that originally exerts an *in vivo* pharmacological activity (Barreiro & Fraga, 2001:237), not necessarily resulting in a drug. Here, its original meaning has been adapted to indicate the strategy of follower firms, managing to explore a successful innovation strategy.

Empirical evidence corroborates the hypothesis that the prices of new medicines are related to product attributes like the degree of innovativeness. Lu and Comanor (1996) analyzed the prices of new pharmaceuticals introduced onto the American market between 1978 and 1987 and compared the mean launch prices of new products with the weighted mean price of already commercialized competing drugs. Their study demonstrated a price level proportional to the degree of innovativeness, as determined by the FDA in its reviewing process[5]. As depicted in table 1, products with major therapeutic advances commanded average prices twice as high as those embodying only modest advances.

TABLE 1: *Prices for New Pharmaceuticals Relative to Those of Existing Drugs (USA, 1978-1987)*

FDA Designation of Therapeutic Advance	Ratio of Launch Prices of New Drugs to Prices of Existing Drugs	
	Acute conditions	*Chronic conditions*
Important advance	2,97	2,29
Modest advance	1,72	1,19
Little/no advance	1,22	0,94

Adapted from Lu & Comanor (1996) in Schweitzer (1997).

As shown in table 2, a similar trend can be derived from the ratio of prices per prescription of new drugs in 1995 and 2000 with prices per prescription of drugs approved before 1995, already commercialized in the USA, by type of innovation as assigned by FDA classification (NIHCM Foundation, 2002).

[5] Until 1992, FDA had a three level ranking system for new drugs approved according to their significance to human health, as described in table 1 (Public Citizen, 2001).

TABLE 2: Average Price per Prescription of New Drugs in Relation to Old Drugs* (USA, 1995 and 2000)

Type of Innovation (FDA classification)[a]	Ratio of New Drug Prices per Prescription to Old Drug Prices per Prescription	
	1995	*2000*
Priority NME	2,64	2,45
Standard NME	1,39	2,20
Priority IMD	1,75	2,26[+]
Standard IMD	1,18	1,74

*Approved before 1995.

[a]FDA classification for new drug applications (NDA), according to active principle – *new molecular entities* (NME) and *incrementally modified drugs* (IMD), for products with already approved compounds – and evaluation of therapeutic potential. A *priority* status accounts for a clinical improvement over available therapies and a *standard* status for no significant clinical improvement.

[+]Value excluding HIV antiviral drugs. Value including HIV antiviral drugs = 3,81

Source: Elaborated based on data from NIHCM Foundation (2002).

In this study from the National Institute for Health Care Management Foundation on the changing patterns of pharmaceutical innovation, based on FDA data, it is worth noting that incrementally modified drugs (IMD) accounted for 60% of new products launched in the USA from 1989 to 2000. When comparing the periods from 1989 to 1994 and 1995 to 2000, IMD accounted for 71% of the growth in product introductions (62% for *standard* IMD). Only 3% of total change came from *priority* new molecular entities (NME) those characterized by the most innovative profile (NIHCM Foundation, 2002).

Further, the mean price per prescription of IMD products relating to older drugs had a significant increase between 1995 and 2000, approaching the price of more innovative drugs (table 2). When including antiretroviral drugs pertaining to the priority IMD category, the price ratio comes to 3.81, superseding the priority NME ratio (table 2).

Those figures reflect the strategy of firms facing the recent trends in the pharmaceutical market: a reduced number of new molecular entities launched worldwide the FDA approved only 17 NME in 2002 and 21 in 2003, compared to an average of 31 for the previous five years (FDA, 2004) and a great number of lead products with expiring patents. New incrementally modified versions of branded drugs are aggresively promoted before patent expiration, persuading

doctors to switch their patients to the new products, transfering brand loyalty and hindering them from generic competition (NIHCM Foundation, 2002). This indicates the importance of product differentiation in drug diffusion and pricing, as new IMD are generally not (much) better therapeutic options, however they are able to command higher prices.

Diffusion of New Medicines, Product Differentiation and Pharmaceutical Marketing

Another important issue to understand regarding the diffusion of new drugs and pricing is *product differentiation*, based on the consumers' *perceptions* of the products' attributes. Hence, differentiation is ultimately derived from subjective factors – even when based on objective data, such as the level of innovativeness – occuring in many possible ways (Losekann & Gutierrez, 2002). For instance, a new medicine may be *considered* a better option for a given therapeutic indication, favoring its adoption, or consumers may prefer the product from an individual producer in place of similar products from competitors. In any case, differentiation affects the identification of product substitutes, constraining competition.

The diffusion of health technology, like medicines for example, has two fases: adoption and use. The former has been historically more extensively studied and addressed by public policy. Among the factors that drive adoption are the characteristics of the technology, of the adopter institutions or individuals and of the environment financing, planning etc. (Banta & Luce, 1993). Product differentiation favours the diffusion of a new drug by means of influencing adoption decisions.

Pharmaceutical marketing aims also at reinforcing product differentiation, in order to maximize market penetration and the ability to set prices. A good example comes from the competition between Tagamet (cimetidine) and Zantac (ranitidine) in the late 1980s. Tagamet, the first H_2-blocker antiulcer agent, was introduced to the American market in 1977, while Zantac, Glaxo's version of an H_2-blocking agent, was launched in 1981. Although it had fewer side effects, the real advantage of Zantac over Tagamet was Glaxo's marketing strategy. They had contracted Hoffman-La Roche to strengthen its capacity to promote its

product worldwide. Despite a 4-year entry lag and a 50% higher price, Zantac's sales increased dramatically, totaling US$ 2.4 billion *versus* Tagamet's US$ 1.2 billion, in 1990 (Schweitzer, 1997:43).

Market competition and medicine pricing

The example above highlights the fact that competition occurs even during the market exclusivity rights of a producer. As discussed previously, this is the case for the introduction of *me-too* drugs and also for products exerting effects through different mechanisms of action, but directed for the same therapeutic use (*eg.* statins and fibrates for treating hyperchloesterolemia). Hence, the characteristics of the specific market segment where a firm is launching a new product modulate its market diffusion strategy, including the introduction price and pricing trends over time. Innovative drugs exert "first movers" advantages, consolidating brand loyalty, which permits them to mantain high prices while retaining considerable market share for many years (Scherer, 1996:371). Followers generally undergo a "penetration" strategy, where drugs are initially priced at lower prices aiming to gain market share, and then the price is raised over time (Schweitzer, 1997:103). One-hundred and forty-eight new drugs were introduced on the American market between 1978 and 1987 (table 1). Their inflation-adjusted prices eight years after product launch were on average 7, 32 and 62 percent higher than the launch prices for drugs in categories of important, modest and little/no therapeutic advance (Lu & Comanor, 1996).

The introduction of generic products after patent (or other market exclusivity rights) expiration undermines the differentiation process. Thus, competition moves toward prices. As a result, there will generally be high demand price elasticity[6] between generic substitutes, but possibly also, to a lesser extent, among chemically different therapeutic substitutes. Ellison *et al.* (1997) describe this phenomenon for the market of oral cephalosporins in the USA.

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[6]Demand price elasticity – or simply demand elasticity – accounts for the variation in the consumption of a good following a change in its price. The more elastic demand is, the more price sensitive is consumption.

Grabowski and Vernon (1996) found a characteristic loss of more than half of market share for branded drugs in the first year of patent expiration between 1984 and 1993 in the American market. On average, drug producers have tended to concentrate on price insensitive consumers[7], thereby reinforcing brand loyalty in order to mantain prices at a profit maximizing level (Scherer, 1996:376-378). Nevertheless, this may not be a typical pattern of generic take-up following patent expiration, as suggested by the multi-country study (USA, UK, Germany and Japan) performed by Hudson (2000). This study shows differences most likely related to legal and regulatory framework, health system organization and market size.

Prices and the demand for medicines

The multifaceted profile of demand for drugs leads to different approaches to the promotion and pricing of products by the pharmaceutical industry. Pricing will vary according to the interplay of features such as regulation and demand market power. There is strong evidence of this pricing trend: in the USA, a great variation on prices paid for the same products among federal purchasers (Medicaid and Veterans Administration), hospitals and Health Maintenance Organizations (HMOs) has been observed (Reidenberg, 2001). Even producers of innovative branded drugs who respond to generic competition through high priced sales (as discussed above) are able to capture some of the price sensitive customers by offering secret discounts to HMOs with aggressive procurement policies (Scherer, 1996:378).

A paradigmatic case of the influence of demand market power on pricing is the evolution of zidovudine prices in Brazil in the 1990s. In spite of generic producers entering the market, a dramatic drop in prices only occured after the establishment of a national AIDS program including universal access to treatment and central procurement of antiretroviral medicines (Oliveira *et al.*, 2000).

When this question is examined focusing on distinct national markets, a rhetorical argument arises: differential pricing according to income level. *Thereby,*

[7] Those can be characterized by risk aversion, imperfect information and/or generous health insurance coverage.

a producer would adapt the price of its product to a profit maximizing point corresponding to the demand elasticity of a particular market, resulting in lower prices in less affluent countries[8]. It implies that contribution of these markets to profits and R&D expenses recovery would be (much) lower than in richer ones, but without their contribution there would be fewer global gains, considering that the producer is acting in the international market[9] (Danzon, 1997). This is the case for the innovative core of the pharmaceutical industry. Nevertheless, there are many exceptions observed in this type of pricing behavior. Some products are more expensive in developing countries than in developed ones and inconsistent price differences exist among developing countries with the same income level (Maskus & Ganslandt, 2002; Balasubramanian, 1998; Bermudez *et al.*, 2001). Considering the previously discussed factors influencing demand, the observed price differences reinforces the notion that prices are set at a maximum value according to market context.

Finally, one should also consider the underlying role of the health care system and of the regulatory background in the interplay of market forces. This may include the registry of pharmaceutical products, including rules for generic product introduction, existence of price control mechanisms, financing of drug prescriptions (whether they are reimbursed, directly supplied or paid by out-of-pocket expenses), regulation of drug prescribing and dispensing, control of pharmaceutical marketing, characteristics of distribution systems and sectoral taxation and fees.

Expected changes following enforcement of TRIPS provisions

A major implication of TRIPS relating to drug prices will be the constraints placed on introducing generic copies of innovative products, which would help contain prices by means of greater competition. This includes not only countries that have local production capacity to generate generic versions but also countries that rely mainly on importation. TRIPS provisions allow countries to adopt some

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[8] An accessible graphical explanation can be found in Scherer & Watal (2001).

[9] Such pricing behavior discriminating markets according to demand elasticity is also referred to as "Ramsey Pricing".

mechanisms in their IP legislation that may permit improved market competition from products similar to patented ones, such as International Exhaustion of Rights[10] (which accounts for parallel importation), Compulsory Licensing, and Early Work Exception[11] (also known as "Bolar Provision"). However, it is not certain whether developing and least developed countries are consistently introducing those provisions into their national legislation. Oliveira *et al.* (2004), studied a representative group of Latin American and Caribbean countries and found that they are not fully incorporating TRIPS flexibilities into their legislation in order to obtain better public health results.

Additionally, there is great concern about whether those countries will have the sufficient political and technical capacity to use such provisions, even if they have been properly addressed by national legislation. Last but not least, there is concern over whether it is economically feasible for generic producers (local or foreigners) to enter their respective markets, considering scale, access to distribution channels, the necessary marketing effort to face innovator competition[12], the grounds under which the patent holder will be financially compensated for a compulsory license and the contingent provision of public policy incentives for producers/importers to supersede these barriers to enter the market.

Through the use of econometric models, there is a small but growing number of studies addressing the impact of introducting patent regimes to lower and middle income developing countries, those which already have significant pharmaceutical industries. The derived estimates indicate a potential increase in prices, ranging from 12% to over 200%, depending on the assumptions on which the models are based (CIPR, 2002:37; Scherer & Watal, 2001).

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[10] This principle considers that the patent owner rights are exhausted with the first sale of the product in the international market. Therefore, one can import the product from a country where its price is lower without infringing patent rights.

[11] Through this provision a generic producer can have access to the documentation used for the registration of the innovative product in order to prepare all necessary procedures to obtain marketing authorization, and in order to launch its product immediately following patent expiration.

[12] Refers to the previous discussion on complementary capabilities and assets for the successful commercialization of an innovation.

Nevertheless, the specific situations resulting from the introduction of new products with different innovative profiles should also be considered, as their effects on the efficiency of pharmaceutical expenditures may vary, distinctly affecting health systems. For instance, one can take the case of the three patented antiretroviral drugs (indinavir, efavirenz, and nelfinavir) which are included in the treatment guidelines of the Brazilian AIDS program due to their effectiveness in HIV infection therapy. These antiretrovirals consume a great amount of the medicines budget. The Ministry of Health has been able to negotiate lower prices for these patented drugs by using the threat of production under a compulsory license, resulting in price reductions ranging from 40% to 65% (Bermudez & Oliveira, 2002; 't Hoen, 2002). These achievements were possible due to visibility of the AIDS problem, public demand, as well as political will to assure program sustainability, and technical capability to produce generic copies of these medicines.

On the other hand, one can consider the case of new non-steroidal anti-inflammatory drugs (NSAIDs), selective inhibitors of the ciclooxigenase-2 (COX-2) enzyme. In Australia there was a large-scale diffusion of such products shortly following its approval, threatening the Pharmaceutical Benefits Scheme (PBS) sustainability by means of an increase in expenses from $76 million by the end of December 2000 to more than $160 million by the end of June 2001 (Dowden, 2003). Evidence shows that celecoxib and rofecoxib have been used beyond the approved indications, often as the first therapeutic option and for patients aged less than 65 years, although COX-2 selective NSAIDs are no more effective than conventional NSAIDs and only those patients with a great risk of developing serious NSAIDs-induced gastrointestinal (GI) complications are likely to benefit from their reduced relative risk (Kerr *et al.*, 2003; National Prescribing Service, 2001). Speculations into the reasons of such prescribing behavior pointed to the influence of pharmaceutical marketing strategies. They sought to reinforce the perception that these medicines had reduced side effects, which was also favoured by the absence of a timely access to independent information. (Dowden, 2003). Although exerting a 50% relative risk reduction of GI complications, the absolute risk of this effect with conventional NSAIDs is as low as 1.4% in the general population and 5% to 0.4% with high- and low-risk patients respectively (National Prescribing Service, 2001).

In Brazil, where these medicines are generally bought by out-of-pocket expenses, sales data show that COX-2 selective NSAIDs have increased their revenues market share in the group of oral NSAIDs from 5% in 1999 to 24% in 2002, undermining the reduction in expenditures achieved by the introduction of generic drugs since 2000. Generic NSAIDs accounted for a revenues market share of 7.85% in 2002 and for a units market share of 14% against 13% for COX-2 selective NSAIDs (Reis & Bermudez, unpublished results).

The above situations highlight the importance of assessing the different scenarios related to the introduction of new patented medicines and how they may represent distinct options for public policies to deal with their effects on health systems. In the case of the new COX-2 selective NSAIDs, for example, it would clearly not be feasible to grant compulsory licenses to reduce prices by means of generic competition, since there are other therapeutic options available. On the other hand, such a situation could be better addressed by policies related to the rational use of drugs, once there is evidence that the diffusion of those products has been driven by a biased perception of their safety and efficacy.

Prices and pharmaceutical expenses: monitoring the effects of patented medicines

As stated from the previous discussion, the effects of patented medicines on health care systems will depend on the therapeutic improvement in association with their respective price level and diffusion pattern, *i.e.* the amount of pharmaceutical expenses they may represent and their respective efficiency. Therefore, an assessment of such effects can only be properly performed by means of analyzing the specific market segments where these products are being introduced, accounting for the characteristics of available technologies, demand, sales, prices and market share of firms.

The identification of the products pertaining to such market segments should be guided by the possibility of substitution among them, in a similar way as in the definition of the *relevant product market* in antitrust regulation (IE/UFRJ, 2002), in order to address competition, including market power and the dynamics of innovation. Identifying the actual competitors in the pharmaceutical market may be challenging, once it means to consider many possibilities of

intersections among products and therapeutic indications. Notwithstanding, one can assume that there are specific areas of competition among products used in the same treatment situations[13]. These markets may be larger than the ones formed by products with a particular active principle or by different drugs showing similar mechanisms of action. On the other hand, they may be narrower than the ones formed by a whole therapeutic class.

Conclusion

This article demonstrates that drug prices are mainly determined by demand factors such as the perception of innovative profile, in terms of clinical improvements, competition in the same market segment and price variation among different classes of buyers.

In any given national market, many of these factors are already in place, irrespective of patent recognition status. However, restraints on introducing generics to the market due to exclusivity rights are likely to reinforce "first movers" advantages of innovative producers, contributing to consolidate innovative firms' market power and hence the ability to determine prices. From a public health perspective, it is useful to understand the patterns of competition, product diffusion and pricing in the pharmaceutical market segments where new, patented medicines are being launched. This will favour the definition of better policy options needed to manage the effects of drug pricing on health care, in order to achieve cost-effective resource allocation and increased access to essential medicines.

[13] As is the case of oral NSAIDs, which include traditional and COX-2 selective NSAIDs, since they have equivalent efficacy as anti-inflammatory agents.

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Chapter 6

WTO TRIPS Agreement Implementationin Latin America and the Caribbean

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In this chapter, a brief overview of the literature that analyzes the TRIPS Agrement implementation processes in developing countries will be presented. Also included is an analysis of the industrial property legislation of some Latin American and Caribbean countries from a public health perspective.

The implementation of the TRIPS Agreement by WTO Member countries almost always requires national intellectual property legislation reform because, without these changes in the legislation, TRIPS has no effect at the national level. Correa (2000) pointed out some fundamental issues that should be considered in the reform of the patent system, which are:

(1) Protection of the environment;

(2) Protection of public health;

(3) Promoting competition;

(4) Promoting technology transfer

(5) Protection of consumers

(6) Support of small local producers; and

(7) Respect of the inventor's rights to be compensated for their contribution to scientific progess

A national patent system that includes the "protection of public health" must be based upon health-sensitive industrial property legislation, that is, the legislation must include all the TRIPS Agreement flexibilities and safeguards that enable governments to efficiently act in the public health sector (Correa, 2000). As mentioned in Chapter 1, the following elements should be incorporated

for health-sensitve patent legislation: adequate transition period, experimental use, parallel importation, compulsory licensing and the Bolar exception.

Bermudez *et al.* (2000) analyzed the recent changes in Brazilian legislation (Industrial Property Law #9.279/96) regarding patent claims and focused specifically on the provisions related to the pharmaceutical and biotechnology sectors, using the number of patent claims from these sectors as the main variable. Notwithstanding the fact that the study only covered a period of two years, the results demonstrated that the main beneficiaries of the recent changes in Brazilian legislation were not Brazilian institutions or companies. Rather, it was the transnational companies who benefited, resulting in their hegemony in the Brazilian market. Chapter 9 contains updated data from 1999-2002.

Thorpe (2001) conducted a descriptive study using data from three important intellectual property regional systems: the African Region Industrial Property Organization (ARIPO), the African Organization of Intellectual Property (OAPI) and the Andean Community. The author analyzed legislation from 70 developing and least developed countries. The objective was to identify the TRIPS Agreement flexibilities and safeguards within the national and regional legislation.

The author found that only three of the 30 least developed countries in Africa are using the transition period to grant patents for products and pharmaceutical processes, as established in the Doha Ministerial Declaration[1]. Also, few developing countries are implementing all of the TRIPS Agreement flexibilities. The analysis shows that all countries included some form of compulsory licensing in their legislation to prevent abuse of industrial property rights.

Keyla (2003) examined industrial property legislation from India, Indonesia, Sri Lanka and Thailand. The study focuses on safeguards that enable governments to take measures to protect public health and describes the health situations of these countries, as well as the political context and the pharmaceutical industry profile.

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[1] The Ministerial Doha Declaration on TRIPS Agreement and Public Health (WTO, 2001) established in paragraph 7 that least developed countries could extend the transition period for pharmaceutical products and processes until 01/01/2016.

The results show that there are many public health problems and that government resources are limited to meet health needs, especially in the context of the WTO TRIPS Agreement. The author up holds the importance of using compulsory licensing to take measures that could favor access to medicines, specially if there exist abuse of patent holder rights, anti-competitive practices, and failure to obtain a voluntary license. The author also highlights the importance of improved relationship between health policy, pharmaceutical policy and patent legislation.

Oliveira *et al.* (2004) analyzed industrial property legislation from 11 countries in Latin America and the Caribbean: Argentina, Brazil, Bolivia, Colombia, Equador, Honduras, Mexico, Panama, Peru, the Dominican Republic and Venezuela. The concept of health-sensitive industrial property law, as established by Correa (2000) was used in the analysis. The study focused on the identification of patentable subject matter, patent term, transition periods, reversal of the burden of proof, exhaustion of rights, compulsory licensing and the "Bolar exception". The TRIPS Agreement flexibilities and safeguards and their impact on access to medicines policy are described. Most countries did not fully incorporate these safeguards and flexibilites.

Industrial property legislation reform in Latin American and Caribbean countries

The methodology used by Oliveira *et al.* (2004) was adapted to study industrial property legislation in other Latin America and Caribbean countries. National legislation for each country was obtained from the WTO website (WTO, 2003).

Until May 2004, the Bahamas, Chile and El Salvador had still not adapted their legislation to the TRIPS Agreement standards. It was not possible to obtain the legislation from the following countries: Antigua, Bermuda, Cuba, Dominica, Grenada, Guyana, Haiti, Jamaica, St. Kitts/Nevis, St. Lucia, St. Vincent/the Grenadines and Suriname. Legislation from Barbados, Belize, Costa Rica, Guatemala, Nicaragua, Paraguay, Trinidad and Tobago and Uruguay were analyzed.

The following TRIPS Agreement flexibilities and safeguards were considered (1) transition period to grant patents for pharmaceutical products

and processes, (2) compulsory licensing, (3) experiemental use, (4) exhaustion of rights, (5) early working (Bolar exception) (6) patent term, and (7) grounds to issue a compulsory license. The definitions of these terms are described in Box 1.

BOX 1: Brief description of the TRIPS Agreement terms, flexibilities and safeguards

PROVISIONS AND MECHANISMS	DESCRIPTION
TERM OF PROTECTION (The lifetime of a patent)	A minimum term of 20 years for all product and process patents, measured from the date on which the patent application was filed. (Art. 33)
PATENTABLE SUBJECT MATTER	Patents shall be available for any inventions, whether products or processes, in all fields of technology, provided that they are new, involve an inventive step and are capable of industrial application (Art 27)
TRANSITION PERIODS	One-year (until 1996) for developed countries Five years (until 2000) for developing countries Eleven years (until 2006) for least developed countries (Art. 65 and 66)
TRANSITION PERIODS FOR PHARMACEUTICALS	Ten years (until 2005) is allowed for developing countries to grant patent protection to fields of technology not protected before January, 1995 (Art. 65.4). The Declaration on TRIPS Agreement and Public Health, 2001 establishes an additional period (until 2016) for LDC countries
EXPERIMENTAL USE	The patent shall not prevent experimental use of the invention by third parties for scientific purposes or for commercial purposes that do not unreasonably conflict with a normal exploitation of the patent and that do not unreasonably prejudice the legitimate interests of the patent owner, taking into account the legitimate interests of such third parties (Correa 2000)
EXHAUSTION OF INTELLECTUAL PROPERTY RIGHTS	According to the theory of exhaustion of intellectual property rights, the exclusive right of the patent holder to import the protected product is exhausted, and thus ends, when the product is first launched on the market. When a State or group of States applies this principle of exhaustion of intellectual property rights within a given territory, parallel importation is authorized to all residents in the State in question (Article 6)
PARALLEL IMPORTS	Products imported into a country without the authorization of the right holder in that country, which have been put on the market in another country by that person or with his consent (Article 6)
COMPULSORY LICENSING	The authorization given by a judicial or administrative authority to a third party for the use of a patented invention, without the consent of the patente holder (Velasquez & Boulet 1999)
EARLY WORKING EXCEPTION (BOLAR EXCEPTION)	This exception allows a country to complete all of the procedures and tests that are necessary to register a generic product before the original patent expires (Article 30)

Source: Oliveira *et al* (2004).

Box 2 shows the WTO entry date and the year of industrial property legislation reform. Of all countries examined, none of them included references regarding the use of the transition period to grant patents in the pharmaceutical sector. As stated in article 65, developing countries have until January 2005 to grant patents on fields of technology not protected before TRIPS. For a more precise analysis of this issue, it is necessary to examine the legislation established and in force before TRIPS.

BOX 2: WTO Entry Date and Patent Legislation Reform

Country	WTO Entry Date	IPR Reform (year)
Barbados	1º January 1995	Patent Act Nº 18/2001
Belize	1º January 1995	Patent Act Chapter 253 /2000
Costa Rica	1º January 1995	Patent Law Nº 7979/2000
Guatemala	21 July 1995	Decree 57/2000
Nicaragua	3 September 1995	Patent Law Nº 354/2001
Paraguay	1º January 1995	Patent Law N° 1.630/2000
Trinidad and Tobago	1º March 1995	Patent Act (Consolidation), 1996 (2000), Nº 21 (Nº 18)
Uruguay	1º January 1995	Patant Law Nº 17 164 /1999

BOX 3: *Implementation of TRIPS Flexibilities and Safeguards in National Legislation*

Country	Compulsory Licensing	Parallel Imports	Early Working (Bolar exception)	Experimental Use
Barbados	+	-	-	+
Belize	+	-	-	+
Costa Rica	+	+	+	+
Guatemala	+	+	-	+
Nicaragua	+	+	-	+
Paraguay	+	+	+	+
Trinidad and Tobago	+	-	-	+
Uruguay	+	+	+	+

Label: + yes; - no.

BOX 4: Levels of Exhaustion of Rights

National Exhaustion	International Exhaustion	Do not have this provision
Trinidad and Tobago	Costa Rica Guatemala Nicaragua Paraguay Uruguay	Barbados Belize

BOX 5: Grounds to Issue a Compulsory License

Country	Failure to Exploit Patent	Public Interest	National Emergency	Remedy for Anti-Competitive Practices	Failure to Obtain License under Reasonable Terms	Dependent Patents
Barbados	+	+*	+*	+*	+	+
Belize	+	+*	+*	+*	+*	+
Costa Rica	+	+	+	+	-	+
Guatemala	-	+	+	+	+	+
Nicaragua	-	+	+	+	+	+
Paraguay	+	+	+	+	+	+
Trinidad and Tobago	+	+*	+*	+*	+*	-
Uruguay	+	+	+	+	+	+

Label: + yes; - no

* Government use

Box 2 shows that, with the exception of Uruguay, all countries used the full transition period of legislation reform.

Box 3 shows the flexibilities and safeguards incorporated into each country's legislation. Costa Rica, Paraguay and Uruguay have fully incorporated all safeguards and flexibilities. Also, these countries included all possible conditions to issue a compulsory license (Box 5). The Bolar exception was the least implemented flexibility, found only in the legislation of Costa Rica, Paraguay and Uruguay.

Compulsory licensing and experimental use were implemented in all countries. International exhaustion of rights is found in Costa Rica, Guatemala, Nicaragua, Paraguay and Uruguay. The legislation of Trinidad and Tobago only includes national exhaustion of rights, while in Belize and Barbados there is no

specification whether exhaustion of rights should be national, regional or international (Box 4).

Box 5 presents the different grounds from which to issue a compulsory license and which of them were implemented in each country. Barbados, Belize, Paraguay and Uruguay incorporated all conditions. Costa Rica, Guatemala, Nicaragua and Trinidad and Tobago incorporated all grounds except for each one.

In conclusion, three of the eight countries- Costa Rica, Uruguay and Paraguay- have public health sensitive legislation since they have implemented all TRIPS safeguards and flexibilities, as well as all of the grounds to issue a compulsory license. The legislation of Trindad and Tobago is in the other extreme, because it only includes the compulsory licensing safeguard. The other countries are in between and have room to improve their legislation by implementing the other flexibilities and safeguards.

Although this study demonstrates that some countries have health-sensitive patent legislation, it is important to point out that the recent bilateral and regional trade agreements or trade relationships between countries have been creating more restrictive patent rules and medicines regulations (TRIPS-plus provisions). For example, due to pressure from United States, Guatemala has changed its IPR legislation (MSF, 2003). In April 2003, the Decree # 9/2003 established five years of protection for data submitted to obtain pharmaceutical product market approval (Guatemala, 2003). This provision, like patent protection, hinders competition, because it creates a type of monopoly for medicines even if they are not protected by patents (Jorge, 2004).

Unfortunately, the Guatemala is not an isolated case. Bilateral agreements have been negotiated and signed between United States and most developing countries worldwide. In this context, policy makers from the health sector have been facing IPR standards beyond those agreed on TRIPS in 1994, which means more obstacles to overcome for implementing access to medicines policies.

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Part II – Intellectual Property Rights and Brazil

Chapter 7

Expanding Access to Essential Medicines in Brazil: Recent Regulation and Public Policies

Jorge A.Z. Bermudez, Maria Auxiliadora Oliveira & Egleubia Andrade de Oliveira

Brazil has been implementing a broad range of initiatives to expand access to medicines, which can provide examples for other developing countries. Of special interest is the universal access to anti-retroviral drugs program that the Ministry of Health established in recent years, which will be discussed below. These initiatives must be considered not as isolated actions but as a sequence of steps that have enabled Brazil's national health system to make advances (Bermudez *et al*., 2000; Bermudez, 2001; 2002, 2003).

This chapter will briefly describe and analyze the most important government policy initiatives of the pharmaceutical industry and access to medicines.

The Central Agency for Medicines (Central de Medicamentos – CEME)

Among other initiatives in the Brazilian health sector, the most important was the creation of the Central Medicines Agency (CEME) under the Office of the President, in 1971. Its functions were defined as regulating the production and distribution of drugs by the pharmaceutical laboratories subordinated or linked to the various government ministries (CEME, 1988; Bermudez, 1992, 1995).

The plan for the Central Medicines Agency included jointly functioning sub-systems: information, production, distribution, research, and evaluation and control. The most relevant measure implemented by CEME during its existence

was to coordinate the official government production system. However, as mentioned in previous studies (Bermudez, 1992, 1995, Bermudez *et al*., 2000, Bermudez, 2002, 2003), CEME catalyzed the conflicts between the public sector and the domestic private sector in pharmaceutical production. The differences between the sectors became increasingly clear in the centralized purchase of medicines by CEME.

CEME was decommissioned in 1997, in the midst of a crisis involving alleged corruption and non-observance of its initial objectives, having become during the years a mere purchaser and distributor of medicines. Its activities had dwindled mainly to the buying of large quantities of medicines from the private sector, while its involvement in research, technological development and the coordination of a national quality assurance system had declined. After being decommissioned, CEME'S activities were reallocated to different departments of the Ministry of Health. This action created the need for an explicit national medicines policy in the Ministry of Health, and was a first step towards establishing the current priorities regarding access to medicines (Wilken & Bermudez, 1999).

Brazilian National Medicine Policy

In the beginning of 1997, a working group was established by the Brazilian Ministry of Health to coordinate the process of a national drug policy, resulting in the first an explicit drug policy consistent with World Health Organization guidelines (OMS, 1998).

After 20 months of negotiations involving different actors, which included health professional representatives, organized society, the pharmaceutical industry, health system managers and international organizations, the Ministry of Health, through MS Ruling # 3.916/98, issued the document entitled "National Drug Policy". This document established the basis and guidelines for activities in this sector, calling attention to the need to link intersectoral actions (MS, 1999a; Yunes, 1999).

The following are the essential guidelines and priorities of the recently formulated National Drug Policy.

Guidelines:

(a) Adoption of a list of essential medicines (EDL);

(b) Health-related regulation of medicines;

(c) Reorientation of pharmaceutical services;

(d) Promotion of rational use of Drugs;

(e) Scientific and technological development;

(f) Promotion of production of pharmaceuticals;

(g) Safety, efficacy, and quality assurance; and

(h) Development and training of human resources.

Priorities:

(a) Permanent review of the National List of Essential Medicines (Rename);

(b) Pharmaceutical services

(c) Promotion of rational medicine use; and

(d) Organization of medicines-related health surveillance activities.

Review of the National List of Essential Medicines (Rename)

Following the approval of the National Drug Policy, the National List of Essential Medicines was reviewed – the last updating had been in 1982. The revision was based mainly on the WHO's Model List for Essential Medicines and on evidence-based, a broad revision of publications on meta-analysis and clinical trials[1]. It was officially adopted as Ministry of Health Ruling # 597/99, and has been distributed throughout the health system. States and municipalities are being encouraged to use similar lists at their own level.

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[1] The classification of all the medicines on the list was made in accordance with the WHO Model List in order to make it easier to use by health system professionals, including general guidelines for disease treatment as well as the medicines used for treatment of systemic organic diseases

In 2001, the Ministry of Health set up a national commission that is responsible for the standing revision of the National List of Essential Medicines[2]. The current essential medicines list in Brazil is composed of 312 items and 561 presentations. Of these, 43.1% are injectables (including all the vaccines and serum), and 24.6% of all the medicines are intended for hospital use.

Following the National List of Essential Medicines, a therapeutic formulary, including guidelines and evidence-based information for essential medicines, was also developed. It is meant to be a guide for rational prescribing within the health services, and not to be restricted to the public sector (MS/ANVISA, 2002).

The Basic Pharmacy Program

The Basic Pharmacy Program (PFB) was established in 1997 to initially provide access to lower-income population groups from poorer areas of Brazil to 40 essential medicines, thus complying with the Constitutional measure ensuring the right to health for all citizens (MS, 1997).

The program was based on the identification of one of Brazil's most serious public health problems, i.e., treatment non-compliance, dropout, and lack of continuity of treatment, due to the fact that patients cannot afford to purchase prescribed medicines. This, leads to the recurrence and aggravation of diseases that could be cured or controlled by prophylactic measures (Folha de Manguinhos, 1997).

The Basic Pharmacy Program consisted of a standard kit of medicines of more general use and was distributed evenly among selected municipalities (counties) of Brazil. Items, in amounts calculated to cover the needs of 3,000 individuals, were distributed for a mean period of three months. Specific drugs were selected for the program to facilitate effective, lower-cost treatment of the most common diseases affecting the Brazilian population, based on prior experience with CEME and the pharmaceutical care programs in the states of Paraná, São Paulo, and Minas Gerais. The drugs were also selected based on the possibility of production by government laboratories. Quantitative estimates of the drugs were performed using mean-consumption-per-treatment criterion,

[2] A second revision was finalized in 2002.

based on standard treatment protocols used for the most common out-patient situations (MS, 1997).

Due to financial limitations, counties with fewer than 21,000 inhabitants were selected, and the plan was to serve 4,199 counties, covering a population of 35,511,679 individuals, at an annual cost for purchase and distribution of the medicines estimated at R$111,288,592.00 (R$3.1339/person/year)(Cosendey, 2000).

The Basic Pharmacy Program was centrally planned, with a fixed range of drugs and did not provide for replenishment of stocks or adjustment of demand for given drugs, with no regard for potential regional specificities or a well-defined role for the State administrative level. Since the selection criterion was number of inhabitants, a certain problems arose in its implementation. The program received criticism from counties that failed to receive the drugs, despite their health conditions being virtually identical to those that were benefited by the program.

Although the Basic Pharmacy Program was conceived to rationalize the distribution of a range of medicines to treat the country´s most prevalent diseases, in practice there were flaws in the links with the State health departments. In addition, at least in its initial stage, no provision was made for strengthening or consolidating the local health services that received the medicines, i.e., with a view towards more rational use. It is important to apply indicators for drug prescribing, dispensing, and use in the various health care units as a basis for evaluating pharmaceutical care policies.

The implementation of the Basic Pharmacy Program by the Ministry of Health highlighted the need for essential drug programs to be operationally linked, and for each State to have a program or plan involving its respective counties, linked politically at the various management levels. In the Brazilian case, these are the so-called Bipartisan Inter-Administrative Commissions. In the current stage of the Brazilian health care system, characterized by a decentralization process, it is necessary to consolidate the State levels in order for them to be capable of implementing clear policies, involving all of their respective counties.

Decentralization of Basic Pharmaceutical Services

Ministry of Health Ruling # 176/99 sets criteria and prerequisites for counties and States to qualify for Basic Pharmaceutical Services, in addition to setting values for Federal government resources. The Ruling also defines the minimum values to be allocated as counterpart contributions at the State and county level.

As part of this current decentralization process involving resources for basic pharmaceutical care in Brazil, some States have opted to totally or partially maintain a centralized administration of State programs, with a fixed list of drugs to be supplied to the counties, based on population criteria. Some counties (or municipalities), especially those with larger populations and which are operating their health systems with the so-called "full management" approach[3], may choose to receive the funds to make their own pharmaceutical purchases.

The issues leading to the decentralization process have been discussed since 1997, covering various aspects relating to drug supply by the Unified Health System (SUS), the demand for drugs by the Ministry of Health, and the consequences of the decommissioning of the Central Medecines Agency (Conass, 1999).

An important report was approved by the Conass (National Council of State Health Secretaries)Assembly in Brasília on March 27, 1998 and was subsequently supported by the Tripartite Inter-Administrative Commission, entitled, "*Towards a Decentralized Pharmaceutical Services Program: a proposal by the Conass based on experiences at the State level*". This report is the first real step towards defining minimum requirements for establishing a decentralized model capable of promoting access to medicines for basic health care. The report is in accordance with Basic Operational Norm # NOB SUS 01/96, the National Drug Policy and other legislation related to pharmaceutical services.

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[3] An accreditation system for municipal (county) health departments according to health system management conditions as defined by the Ministry of Health's Basic Operational Norm # NOB/96 (MS, 1997)

The National Health Surveillance Agency

The National Health Surveillance Agency (ANVISA) was created through Act # 9.782/99 in January 26, 1999. Its main purpose is to foster protection of the health of the population by exercising sanitary control over production and marketing of products and services subject to sanitary surveillance. The Agency is part of the Ministry of Health but has administrative and financial autonomy. This means it is an independently administered, financially-autonomous regulatory agency, with guarantee of tenure for its directors during the period of their mandates. ANVISA is managed by a Collegiate Board of Directors, composed of five members. It was created along the lines of the American Food and Drug Administration, for regulating health-related products and services, replacing the previous body in the Ministry of Health that had that responsibility (Bermudez *et al.*, 2000; ANVISA, 2004a).

The agency has incorporated additional responsibilities, such as coordination of the National Sanitary Surveillance System (SNVS), the National Program of Blood and Blood Products and the National Program of Prevention and Control of Hospital Infections. ANVISA also: monitors drug prices and prices of medical devices; is responsible for issues pertaining to regulation, controls and inspection of tobacco products; provides technical support to the National Institute of Industrial Property in granting patents for the pharmaceutical industry (ANVISA, 2004a). The Agency also has control over ports, airports and borders as well as liaisons with the Brazilian Ministry of Foreign Affairs and foreign institutions over matters concerning international aspects of sanitary surveillance.

Therefore, Act # 9.782/99 marked the beginning of the implementation of a new regulatory system for medicines, foods, sanitary products, cosmetics and other areas of sanitary surveillance. With this Act, the federal government reorganized the national surveillance system, which was previously considered inefficient and corrupt. The creation of ANVISA resulted in the implementation of a series of administrative, technical and financial changes. New taxes and mechanisms were created to make sanitary surveillance self-sufficient (Gemal, 2004).

The Generics Act

Despite several previously unsuccessful attempts at implementation, the Executive Branch enacted Act # 9.787/99, amending Act # 6.360/76, which dealt with various facets of licensing and inspecting products and services, establishing the basic concepts and effectively introducing generic drugs in Brazil. Supplementary measures, especially Decree # 3.181/99 and Resolution # 391/99 of ANVISA, regulated various aspects in the implementation of generic drug policy in Brazil, such as establishing technical standards and norms and defining the concepts of bioavailability and bioequivalence for generic, innovative, reference, and similar medicines. ANVISA also set the criteria and conditions for licensing and controlling generic drugs in the Brazilian pharmaceutical market.

The regulation of generic drugs sparked a controversy with widespread media coverage, in light of the break with established hegemonies in the Brazilian market. The implementation of the generic Act in Brazil met resistance from the Brazilian transnational pharmaceutical companies association (ABIFARMA). Aiming to undermine the reliability of generics, ABIFARMA developed campaigns directed towards both to consumers and physicians. The reason was the expansion of sales by domestic manufacturers of generic medicines, which led to transnational market share loses (Fritsch, 1999).

The Act # 9.787/99, known as the "Generics Act" defines what is considered a generic medicine and under which conditions generic names may be used for pharmaceutical products in Brazil (Brazil, 1999). A generic medicine is defined as a product similar to the reference or innovator[4] product, and is expected to be interchangeable[5] with the latter. Generics are usually produced after the expiration or waiver of patent protection or any other exclusive rights. Safety, quality and efficacy must be proven according to Brazilian Non-Proprietary Name (DCB) standards, or in the absence of DCB approval, by International Non-Proprietary Name (INN) standards. To obtain commercial licensing, these medicines must be approved for safety, efficacy and quality and must be

[4] Reference drug product - innovator product registered at the federal agency in charge of sanitary surveillance and marketed in the country. Effectiveness, safety and quality have been scientifically proven to the federal agency, upon registration.

[5] Interchangeable Pharmaceutical Product - therapeutic equivalent to a reference drug Product, the same effectiveness and safety standards are essentially proven.

interchangeable to the reference medicine. This means that comparative tests to prove pharmaceutical equivalence and bioequivalence[6] are mandatory.

The Generics Law created a new category of copies of commercialized medicines in Brazil, called similar medicines, which until May 2003, were registered only using the criteria of similarity. In other words, proving interchangeability was not required. Similar medicines contain the same: active ingredients, concentration, dosage form, routes of administration, dose regimen, therapeutic indication-preventive or diagnostic-of the reference medicine. They are registered in the ANVISA, however, most of them are not considered interchangeable to the reference drug, because they are not submitted to comparative tests of bioequivalence. Similar medicines can only be marketed by brand name. In summary, Brazil has three categories of medicines in circulation: the innovative, which have brand names, and may be patented or not; generic versions that use DCB or INN standards and are interchangeable with their respective reference medicines; similar medicines, that also have brand names and are similar to the reference drug, but are not submitted to tests of bioequivalence. ANVISA rules # 133/03 and 134/03 (ANVISA, 2004b, 2004c) establish new requirements to obtain market approval for similar medicines, which include the need to perform "relative bioequivalence" tests to compare with a reference drug. This means that during the next five years all similar medicines commercialized in Brazil will have to be submitted to bioequivalence testing.

One of the objectives of Brazilian generic policy is to promote competition between medicines, in their different relevant markets, aiming to reduce prices especially for medicines for chronic conditions.

The implementation of generic policy has enabled the strengthening of the local pharmaceutical industry. According to data from the Association of the Brazilian Generic Medicines Industry – (Pró-Genéricos, 2004), in the last three years, the generic industry invested close to R$ 1 billion in the construction and modernization of Brazilian industrial plants. Currently, 80% of the medicines units marketed in the country are locally produced and Brazilian companies

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[6] Bioequivalence - the demonstration of pharmaceutical equivalence between products presented in the same dosage form, containing identical composition of drug(s), and that have comparable bioavailability when studied under the same experimental design (Act # 9.787/99).

account for 74.6% of the total value of sales. It is important to note that large international generic industries are building their capacity for local production. This is reflected in their increasing market share participation. Indian companies are responsible for 10.3% of the generic market share, followed by German 4.7%, Swiss 4.6%, American (US) 3.8% and Canadian 2%. Today, the four biggest companies in this sector are supported by national capital, as shown in Table 1.

TABLE 1. Top ten local manufacturers of generic medicines by volume of sales and participation in the market.Brazil, 2004

COMPANY	VOLUME OF SALES (# of packages)	PERCENTAGE OF GENERIC MARKET SHARE
MEDLEY	1.79 Million	24.11%
EMS SIGMA PHARMA	1.78 Million	21.00%
BIOSINTÉTICA	1.12 Million	14.58%
EUROFARMA	907 Thousand	10 54%
RAMBAXY	435 Thousand MIL	10.04%
APOTEX	267 Thousand MIL	4 56%
MERCK	206 Thousand MIL	3.07%
NOVARTIS	170 Thousand MIL	4 30%
HEXAL	104 Thousand MIL	1.88%
MEPHA	100 Thousand MIL	0 04%

Source: Pró-genéricos, 2004

The first generic drug approvals in Brazil were issued in February 2000. Four years later, 1140 approvals were issued for 270 active ingredients, corresponding to 4,448 dosage forms. These medicines are manufactured by 53 pharmaceutical companies, of which 27 are national and 26 are international, as described in Table 2 (Bermudez *et al.*, 2000, Bermudez, 2001, ANVISA, 2004d). In Brazil, licensed generic products pertain to 57 pharmacological groups of medicines, including those for in-patients and out-patient use. ANVISA is also aware of the differences in price of new products coming into the Brazilian market, since it is not acceptable to introduce more expensive drugs. For this reason, generic products must be nearly 40 per cent cheaper than the reference products, which are mostly branded products from big transnational companies whose patent protection has expired.

TABLE 2: Pharmaceutical Companies by Origin of Capital and Number of Generic Medicines Registered by ANVISA, Brazil, 2004

PHARMACEUTICAL LABORATORY	ORIGIN OF CAPITAL	# OF REGISTERED MEDICINES
EMS	NATIONAL	166
EUROFARMA	NATIONAL	121
MEDLEY	NATIONAL	108
RAMBAXY	FOREIGN	89
PRATI-DONADUZZI	NATIONAL	66
TEUTO	NATIONAL	61
BIOSINTÉTICA	NATIONAL	48
APOTEX	FOREIGN	44
NOVARTIS	FOREIGN	37
NEOQUÍMICA	NATIONAL	36
MEPHA	FOREIGN	35
CRISTÁLIA	NATIONAL	34
BRAINFARMA	FOREIGN	33
HEXAL	FOREIGN	33
ABBOTT	FOREIGN	32
NATURES´S PLUS FTCA	NATIONAL	28
MERCK	FOREIGN	21
UNIÃO QUÍMICA	NATIONAL	17
ATIVUS	FOREIGN	11
ABFARMO	FOREIGN	10
CINFA	FOREIGN	10
GREEN PHARMA	NATIONAL	10
ALCON	FOREIGN	09
PRODOTTI	FOREIGN	08
ASTA MEDICA	FOREIGN	07
DUCTO	NATIONAL	06
HIPOLABOR	NATIONAL	06
ARROW	FOREIGN	05
HYPOFARMA	NATIONAL	05
HALEX ISTAR	NATIONAL	05
BRISTOL	FOREIGN	04
IPCA	FOREIGN	04
SANVAL	FOREIGN	04
KINDER	FOREIGN	03
THEODORO F SOBRAL	NATIONAL	03
ALLERGAN	FOREIGN	02
BIOLAB SANUS	FOREIGN	02
LUPER	FOREIGN	02
ALTANA FARMA	FOREIGN	01
BIOBRAS	FOREIGN	01
BUNKER	NATIONAL	01
CELLOFARM	FOREIGN	01
EQUIPLEX	NATIONAL	01
ESTERLINA	NATIONAL	01
GENON	NATIONAL	01
KNOLL	FOREIGN	01
JP	NATIONAL	01
LAFEPE	NATIONAL	01
LIBBS	FOREIGN	01
NOVAFARMA	NATIONAL	01
VITAPAN	NATIONAL	01
RIOQUÍMICA	NATIONAL	01
ZAMBON	FOREIGN	01
TOTAL		1140

Source: ANVISA, 2004d."

No strict price controls on generic medicines are being implemented, but the Ministry of Health has proposed two lists of priority products that are be strongly encouraged to have generic versions. These lists are based on the WHO's Model List for Essential Drugs, the Brazilian Essential Drugs List, basic health care lists of drugs in the Brazilian health system and on considerations of the market share of medicines. These two lists have had positive reactions from manufacturers, and requests to license generic drugs have been granted (Bermudez *et al.*, 2000; Bermudez, 2001; Bermudez, 2002). The market share of generic medicines is around 10% of the total medicines market in number of units sold, and 5% of the value(ANVISA, 2004e). Generic industry expectations are to achieve a 30% market share of the number of units sold by the year 2007 (Pro-genéricos, 2004).

State-owned pharmaceutical manufacturers

An important characteristic of the Brazilian pharmaceutical industry is the existence of a network of public laboratories which produce medicines and biologicals to supply the public health system at the three levels of government (federal, state and municipal levels).

This network is composed of 18 laboratories, established in different public administration entities such as the Ministry of Health, the Armed Forces, state governments and universities. Existing production capacity is estimated at 11 billion pharmaceutical units per year. Laboratory distribution by region is organized in the following way (ALFOB, 2003)[7]:

Northeast Region

State Pharmaceutical Laboratory of Pernambuco –L AFEPE

Pharmaceutical Laboratory of Alagoas – LIFAL

State Pharmaceutical Laboratory of Paraíba – LIFESA

Center for Research on Food and Medicines (RN)– NUPLAN

[7] A laboratory linked to the Federal University of Amazonas, in the Northern region of the country, is in its final stages of installation (MS, 2003).

College of Pharmacy, Dentistry and Nursing – UFC – FFOE

Pharmaceutical Technology Laboratory – UFPB – LTF

Southeast Region

Institute of Technology in Medicines – FARMANGUINHOS

Ezequiel Dias Foundation – FUNED

Foundation for Popular Medicines – FURP

Vital Brazil Institute – IVB

Air Force Chemical and Pharmaceutical Laboratory – LAQFA

Navy Pharmaceutical Laboratory – LFM

Army Chemical and Pharmaceutical Laboratory – LQFE

Southern Region

Pharmaceutical Laboratory of Rio Grande do Sul – LAFERGS

Pharmaceutical Laboratory of Sta. Catarina – LAFESC

Laboratory of Teaching and Research in Medicines and Cosmetics – LEPEMC

Medicines Production Laboratory – LPM

West-Central Region

State Chemical Company of Goiás – IQUEGO

The production of these public laboratories represents close to 3% of national production in monetary value and 10% in unit numbers, corresponding to almost 10% of total medicine purchases by the Ministry of Health (MS, 2003).

TABLE 3: Public Laboratory Production/Pharmaceutical Units/2003

LABORATORY	PRODUCTION VOLUME
FURP	3,903,840,000
LIFAL	1,728,144,000
LAFEPE	1,345,680,000
FARMANGUINHOS	1,289,067,280
FUNED	692,340.000
IQUEGO	618,000,000
LAFERGS	375,800,000
LAQFA	242,352,000
LQFE	209,419,590
LTF	193,080,000
LFM	120,800,000
LPM	96,000,000
LIFESA	80,000,000
LAFESC	38,400,000
LEPEMC	21,000,000
IVB	10,680,000
FFOE	7,200,000
NUPLAM	876,320
TOTAL	**10,972,679,190**

Source: ALFOB, 2003

Previous studies (Bermudez,1992;1995)highlighted that strengthening and consolidating production can be an effective instrument in supporting government health policies, which can provide subsidies to regulate prices within the government market. This has occurred in the recent negotiations of antiretroviral (ARV) prices between the Ministry of Health and patent holding transnational laboratories, that threatened to jeopardize the continuity of Brazil's universal access to treatment program for People Living with HIV/AIDS (PLWHA)(as stated in chapter 1).

These price negotiations involved the Brazilian government and three transnational laboratories, Merck, Roche and Abbott. The Institute of Technology in Medicines (Farmanguinhos/Fundação Oswaldo Cruz/Ministério da Saúde) supplied the Ministry of Health with reference information to establish acceptable prices. This was possible because of the Institute´s reverse engineering capability, which enabled the government to threaten with compulsory licensing in the case of a negotiation stalemate (Oliveira *et al.*, 2004).

Medicines produced by the public laboratory network contribute to the financial sustainability of strategic Ministry of Health programs. Another aspect to be considered is the role these laboratories have in research, development and medicine production for diseases prevalent in poor countries, also knows as neglected diseases (Trouiller *et al.*, 2002).

Considering that the amount of private investment into the R&D sector in Brazil is small, the technological development initiatives developed by some of the public laboratories, despite being limited, has presented promising results, especially for ARVs.

In the past three years, due to the importance of the public laboratory network for the viability of strategic Ministry of Health programs, the federal government has invested close to US$20 million to modernize and amplify the industrial production plants (MS, 2003).

Universal Access to Medicines for People Living with HIV/AIDS

Universal access to ARVs in Brazil cannot be analyzed in an isolated fashion. It must be seen as one of the key elements of an integrated program that has been implemented on a step-by-step basis over the years. From 1980 to December 2003, some 277,154 cases of AIDS were reported to the Ministry of Health, leading to the estimate that 597,000 Brazilians were infected with HIV (MS, 2003). As of January 2003, 125,000 PLWHA were receiving ARV treatment, which correspond to 100% of those in need (MS, 2004).

The Brazilian Ministry of Health's policy and guidelines for care of PLWHA has legal support. In addition to the regulations of the Constitution and the health system, Act # 9.113/96, passed in 1996, guarantees every patient free access to all medicines required for treatment (Brazil, 1996). Standard treatment guidelines are set forth and reviewed at least once a year under the sponsorship of the Ministry of Health (MS, 2001; Oliveira *et al.*, 2002; Bermudez 2003)

The Brazilian health services network for providing treatment for PLWHA, including ARVs, is composed of a total of 2,015 units: 1,126 STI outpatient services, 381 other outpatient units, 54 homecare services, 79 day care health services and 375 accredited hospitals. Medicines are dispensed in all states in a total of 424 pharmacies, most located in the health services network. Laboratory support

for diagnosis of the infection and monitoring treatment is carried out by 73 laboratories, which have the capability to measure viral loads, and 65 have the capability to do CD4/CD8 counts. In addition, twelve laboratories are responsible for viral resistance surveillance (MS, 2002).

From 1991 to 1995, the provision of ARV treatment in Brazil had a limited range because of the insufficient supply and availability of medicines in the public health network. In 1996, intensive media coverage of new technologies, availability of efficacious protease inhibitors and the ability to combine medicines into "cocktails", led to a more comprehensive approach and the creation of Ministry of Health guidelines (Oliveira, 2001). From 1996 onward, the Ministry of Health ensured an increased supply of drugs, and the first Brazilian consensus on the use of ARV therapy and Technical Advisory Groups was established. A logistic system for purchase and distribution of medicines was developed as well.

According to the Ministry of Health (MS, 2000), the principles of universal, integral and equal access to care ensure that 100 per cent of patients with HIV/AIDS receive the necessary treatment. The results are dramatic, and respectively include 48% and 49% reductions in the death rate of patients in two studies carried out in São Paulo and Rio de Janeiro. There has been a considerable reduction in hospital admissions since 1997. It has been estimated that approximately 234,000 AIDS-related hospital admissions were prevented in the period 1997–2000, representing an overall savings of US$ 677 million for the health system (MS, 2001).

Currently, the Ministry of Health is responsible for supplying 16 ARVs, including six nucleoside analogue reverse transcriptase inhibitors, two non-nucleoside analogue reverse transcriptase inhibitors, one nucleotide analogue reverse transcriptase inhibitor, and seven protease inhibitors. State governments are responsible for providing medicines for treatment of HIV-associated opportunistic infections (Oliveira *et al.*, 2002).

There exist seven public manufacturers of ARVs in Brazil. Besides Far-Manguinhos, which is a federal manufacturer linked to the Ministry of Health, other state manufacturers producing ARVs include the: Foundation for Popular Medicines; State Pharmaceutical Laboratory of Pernambuco; Pharmaceutical Laboratory of Alagoas; State Chemical Company of Goiás; Ezequiel Dias Foundation and the Vital Brazil Institute. The federal manufacturer, Far-Manguinhos, is

responsible for developing the manufacturing process for the final products, and supplies nearly 30% of all AIDS medicines used in Brazil. Far-Manguinhos is also responsible for developing reverse-engineering technology for pharmaceutical ingredients which strategically support policies of the Ministry of Health (Boechat, 2003).

ARV prices in Brazil have fallen in recent years due to negotiations and centralized procurement with international pharmaceutical companies and the promotion of state manufacturing. According to data from the Ministry of Health, domestic production has reduced ARV prices 78% in average. Negotiation with transnational companies has reduced prices of locally produced ARVs 70%, and of imported products 25% in average (MS, 2001). As demonstrated by a study performed by Oliveira *et al.* (2000), the price of Zidovudine has dramatically fallen during the 10 year period from 1988 to 1999. Government centralized purchases of ARVs was the most important factor that contributed to zidovudine price decrease, as verified by the authors. A cost-benefit analysis has found that, when considering the resources spent on ARV therapy, the savings in hospitalization, welfare and years of life gained are clear. Government support for the AIDS treatment program has been sustained by pressure from a coalition of social forces, the quality of the program and the global importance of the AIDS pandemic (MS, 2000a).

A decrease in the frequency of the most common opportunistic infections has also been reported in Brazil – at a mean rate of 60 to 80% reduction, including Cryptococcus infection (- 60%), CMV infection (- 54%) and Kaposi's Sarcoma (- 38%) – in major centers that receive severely immuno deficient patients. New cases of tuberculosis in HIV+ patients also have decreased (MS, 2001).

Further evidence of the positive aspects of providing universal access to ARVs is provided by the partial immunological reconstruction that is being promoted by treatment. This has been shown by the progressive rise of the main TCD4+ count after 18 months of treatment. This improvement seems to reduce the frequency and severity of opportunistic infections and provides a better quality of life. All of this evidence is a response to the criticism that has frequently been made regarding the poor quality of domestic state production in Brazil publicized at recent forums (Bermudez, 2003).

TABLE 4: Estimated Funds Allocated for Drug Purchases for Ministry of Health Programs . Brazil, 1999-2003. (in R$ 1,000)

PROGRAMS	1999	2000	2001	2002	2003
Incentives for basic pharmaceutical services (decentralized to the state and county levels)	163,947	164,200	168,300	168,300	171,162
High cost drugs	296,357	316,000	449,000	489,539	603,800
Essential drugs for treating mental conditions (decentralized to the State level)	22,178	26,800	24,400	26,800	29,400
Strategic Ministry of Health programs (leprosy, tuberculosis, AIDS, diabetes, blood products, and endemic diseases control)	908,500	806,047	804,537	997,179	1,008,716
TOTAL	**1,390,982**	**1,313,047**	**1,446,24**	**1681,82**	**1,813,078**

Source: MS (Brazilian Ministry of Health), 1999b, 2000, 2001a.

Federal Allocations for Medicine Purchases

The Ministry of Health's annual budget total for 2002 was R$ 24.7 billion. Of this total, more than 10% (around R$ 3 billion) was spent on medicine purchases, including those used during hospitalization (MS, 2002; Cardenas, 2002; MS, 2002). Since the decommissioning of the CEME, in 1997, new pharmaceutical service programs, for basic pharmaceutical services, high cost drugs, essential drugs for treating mental conditions and other strategic programs have been receiving a substantial amount of funds, as described in table 4.

It is important to point out that in addition to the funds allocated at the Federal level or through Ministry of Health transfers, both the states and counties also allocate their own funds either to meet specific demands from their health care systems or to match or supplement funds received from the Federal government.

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Chapter 8

Brazilian Intellectual Property Legislation

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This chapter briefly presents the history of the Brazilian intellectual property rights (IPR) legislation encompassing the period from 1808 to the current days. It also discusses the TRIPS Agreement implementation focusing on recent changes of legislation related to public health protection. Concepts regarding IPR and Public health are not in the scope of this chapter because they are discussed in chapter one.

Background

The first Brazilian Industrial Property legislation was enacted, after the Portuguese Crown was transferred to Brazil, in 1808, in the wake of the Napoleonic Wars in Europe. Previously, Portugal's policy had been to exploit Brazil's natural resources and block any activities in the colony that might jeopardize the Crown's economic, financial, and political interests (Barbosa, 1983). Brazil was the fourth country in the world and the first in Latin America to protect the rights of inventors, by granting patent protection for an invention's novelty and use. This was established by the Royal Portuguese Government, and later charted by the Prince Regent of Portugal and Brazil, in January 28th, 1809. However, even before the Charter was passed, patents had already been granted by the Royal Government (Ben-Ami, 1983).

In 1883, Brazil was one of the 16 countries that signed the Paris Convention, which established the three pilars of the current patent system, which are: independence of patents and trademarks, equal treatment of nationals and

foreigners and priority rights. The Convention, which has articles still in force today, allowed countries to utilize the patent system as an instrument of economic and technological development. Consequently, each country could establish their own IP regime in a way that would favor national policies. The Paris Convention went through many modifications, and in Brazil, the Stockholm version (1967) is currently in force (as stated in chapter 1).

Brazilian Industrial Property Code was based on the experience of late 19th-century Europe, when there was limited employee migration from one company to another and little scientific progress in the fields of chemistry and physics (INPI, 1996).

Before 1945, Brazilian Industrial Property legislation granted patent protection for pharmaceutical products and processes. In that year, the legislation was modified to exclude protection of inventions related to: foodstuffs, medicines, materials and substances obtained by chemical means or processes. In 1969, a change in the Brazilian Industrial Property Code completely eliminated patenting in the pharmaceutical sector, until the current Industrial Property Law # 9.279/96 (Brasil, 1996) was enacted on May 14th, 1996.

Recent IPR legislation reform (1995-2003)

The first wave of reform: 1995 to 1998

The current international intellectual property rights system was built during the Uruguay Round, which was held between 1986 and 1994, within the General Agreement on Tariffs and Trade (GATT). Due to pressure from developed countries, a specific agreement on availability and enforcement of such rights became part of the Round: Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS Agreement). It was signed by 123 countries, in April 1994, in Marrakech. This Agreement sets minimum standards for IPR protection that all WTO Member countries must abide (Correa, 2000).

This was the first time that same intellectual property standards were applied to countries of different social and economic levels. However, in order to enforce these standards, many countries were required to reform their national legislation to comply with the Agreement.

In Brazil, a presidential decree # 1.335/94 institutionalized the TRIPS Agreement during December of 1994 (Brasil, 1994). Less than two years later, the new Industrial Property Law (Law # 9.279/96) was passed on May 14, 1996. Even though, the deadline was set for January 2000.

Unfortunately, the new Brazilian industrial property law did not implement all of the TRIPS Agreement flexibilities and safeguards, which favor health policy (Oliveira *et al.*, 2004). For example, the first version of Law # 9.279/96 only included some of the flexibilities and safeguards, such as compulsory licensing, experimental use and limited use of parallel imports.

Brazil was subject to strong international pressures, especially from the United States, to reform its Industrial Property Law in order to grant patents for pharmaceutical products and processes. For example, the US instated trade sanctions on 100% of all Brazilian exports in other sectors, such as paper, chemical and electrical products until Brazil drafted industrial property legislation with the required changes (Tachinardi, 1993).

Law # 9.279/96 introduced major changes, including patent protection for pharmaceutical products and processes, consistent with Article 27 of the TRIPS Agreement. Brazil did not use the full transition period - until January 2005 - to grant patents in this sector, as established in Article 65. Instead, Brazil began granting patents in the pharmaceutical industry in May 1997.

The law also included *Pipeline* protection (articles 229, 230 and 231), as specified in Article 70.8 of TRIPS. This article requires countries to have an adequate infrastructure for receiving and filing patent applications from the date of enforcement of the Agreement.

According to Velasquez and Boulet (1999):

> "*Pipeline protection is a kind of retroactive protection, to the effect that pharmaceuticals already patented in other countries but not yet patented in the "pipeline" country (because its legislation did not grant patents for pharmaceuticals), nor marketed in that country, may be claimed for protection as soon as the Agreement comes into force. However, the TRIPS Agreement imposes protection only on inventions still meeting the criteria for patentability (notably because they have not yet been disclosed) on the date of entry into force of the Agreement*".

Developed countries, such as the United States, England, Germany, Japan, and France, benefited most from the use of *Pipeline* protection. For example, 45% of the total number of *Pipeline* patent claims were from the United States and only 1.4% were from Brazil (Bermudez *et al.*, 2000).

The flexibility of parallel imports is consistent with the concept of international exhaustion of rights. The patent holder's rights are exhausted when the licensee places the product on the foreign market. Thus, any person may import a patented product, even for commercial purposes, as long as it has been placed on the foreign market by the patent holder or with third-party consent. (Bermudez *et al.*, 2000; Oliveira *et al.*, 2004). Additionally, in Article 43(IV) of Brazilian legislation, national exhaustion of rights is permitted. This means that it is not possible to import a patented product that has previously been commercialized by the patent holder or an authorized third party in another country at a lower price.

Compulsory licensing permits the use of a patented product or process without prior authorization of the patent owner under several conditions. Article 31 of the TRIPS Agreement and Chapter VIII, Section III, articles 68-74 of Law # 9.279/96 describe these conditions. In Brazilian law, a compulsory license can be issued for the following grounds: failure to exploit patent; public interest; national emergency; remedy for anti-competitive practices; failure to produce locally and dependent patents (Oliveira *et al.*, 2004).

Experimental use is a flexibility related to research, allowing use of the invention without compensation for the patent holder. As stated by Correa (2000): "An experimental use exception may foster technological progress based on 'inventing around' or improving a protected invention, as well as permit evaluation of an invention in order to request a license, or for other legitimate purposes, such as to test whether the patent is valid".

The second wave of reform: 1999 to 2003

During the 1990s, patent legislation reform was done with little participation from health sector professionals. Their contribution could have resulted in the development of a more public health-sensitive legislation. In 1999, for example, Decree # 3.201 was established to address compulsory licensing in cases of national emergency and public interest, further described

in Art. 71 (Law # 9.279/96). This article established that, "In cases of national emergency or public interest declared by the Federal Government, temporary and non-exclusive compulsory license can be issued if the patent holder or licensee is not sufficiently exploiting the patent, without infringing upon the holder's rights". Nevertheless, this Decree restricts the full use of Compulsory Licensing in these cases because it contains additional procedures not included in article 71, which create implementation obstacles. An example of this problem is found in article 10 of the Decree, which establishes that any product issued a compulsory license can only be imported from a country where it was marketed by the patent holder or by authorized third parties. This means that countries not granting patents in the pharmaceutical industry were not able to export cheaper generic medicines to Brazil. One example of this situation is India. It opted to use the full transition period to grant patents in the pharmaceutical sector until the year 2005 and currently has a large generic production capacity.

In 2001, in order to reduce ARV prices to sustain the Brazilian Program of universal and free access to treatment for People Living with HIV/AIDS (PLWHA), the Brazilian government held negotiations with three multinational pharmaceutical companies. These negotiations demonstrated some weaknesses regarding protection of public health in Law # 9.279/96. These negotiations demonstrated some weaknesses regarding protection of public health in Law # 9.279/96, especially concerning the lack of the Bolar exception and the absence of involvement by the Brazilian National Health Surveillance Agency (ANVISA) in the process of granting patents in the pharmaceutical industry. As result, in order to address public health interests, Law # 10.196/2001 was enacted as an amendment that modified articles 43 and 229 of Law # 9.279/96.

Article 43, which describes the limits of rights conferred to the patent holder (Exception to Rights Conferred), was altered to include the Bolar exception (early working). This flexibility allows a company to complete all of the procedures and tests that are necessary to register a generic product before the original patent expires (Article 30) (Correa, 2000). Therefore, the Bolar exception allows immediate marketing of generics after patent expiration, thus promoting competition with the innovator medicine, which can lower prices.

The amendment of Law # 9.279/96 also modified articles 229, 229-A, 229-B and 229-C. Article 229-C establishes that the ANVISA must be consulted before a patent can be granted for pharmaceutical products and processes. In

other words, ANVISA is responsible for determining if the novelty requirement is truly satisfied.

It is common practice for the pharmaceutical industry to make small changes to patented products, even though this does not qualify as a novelty. Usually, the validity of these new patent claims is null and deserves a more critical analysis by an institution like ANVISA to avoid extending monopolies without justification. This practice includes patent claims for pharmaceutical forms, analogue processes, combinations of known products, optical isomers, active metabolites, pro-drugs, new salts, and second use (Correa, 2001).

In 2003, during another round of ARV price negotiations, further weaknesses were identified in Brazilian industrial property legislation. As mentioned before, some articles of Decree # 3.201/99 represented additional obstacles in order to issue compulsory licenses for medicines, particularly when considering importation.

In September 2003, some articles from this Decree were modified by Decree # 4.830/03 (Brasil, 2003). A new version of article 10 allows importation of the object under compulsory license also from countries where the product is not patented. Therefore, Brazil has the right to import products from any country including those still using the transition period for pharmaceuticals, like India.

In the ARV price negotiations described previously, Brazil was able to threaten to issue a compulsory license because of the recent changes made in the IPR legislation (Law # 10.196/2001 and Decree # 4.830/03). In January 2004, an agreement was reached between the pharmaceutical companies involved, and as a result, the Ministry of Health was able to save R$ 299 million, representing 37% of the total ARV budget. The savings obtained through this agreement enabled 20,000 new patients to enroll into the AIDS program and also allowed for two additional ARVs to be included: Tenofovir (Gilead) and Atazanavir (Bristol) (MS, 2004).

Despite the above described public health sensitive changes, implemented into Brazilian IPR legislation during this period, a step back occurred with the enactment of Law # 10.603 on December 17, 2002, This Law allowed for the protection of undisclosed data submitted by pharmaceutical companies to national regulatory authorities in order to obtain marketing approval for

veterinary pharmaceutical products, fertilizers as well as agrotoxics and their components (Brasil, 2002). As discussed in previous chapters (2 and 6), this provision has been included in recent bilateral agreements between US and several developing countries worldwide. In fact, these agreements constitute part of the US strategy to create more restrictive IPR regimes than those previously established by TRIPS Agreement (Jorge, 2004).

The Law establishes different terms for data protection, which are dependent on product and information characteristics. Data protection is guaranteed for a ten year period after the approval if the product includes a new molecular entity, either chemical or biological, and if no product information has been disclosed in any country. A five year period of data protection is granted when the product does not contain a new molecular entity and if no information has been disclosed.

As mentioned in chapter 6, this provision, like patent protection, hinders competition. It creates a type of monopoly for medicines, even when they are not under patent protection. The following boxed text briefly describes the historical trends in Brazilian industrial property legislation (Epsztejn, 1998; INPI, 1996; Cerqueira, 1982).

a) Ruling # 28/01/1809: constitutes the initial framework for the development of industrial property rights in Brazil.
b) Imperial Constitution, March 25, 1824: ensures inventors' ownership rights over their discoveries and production.
c) Law of August 28, 1830, regulates the Imperial Constitutional norm and implements legal protection for inventors' rights.
d) Decree # 2.712/60: clarifies instructions for enforcement of the Law of August 28, 1830 and declares that the term of patent protection should begin on the date the patent is granted, not the date it is applied for.
e) Announcement of January 22, 1881: provides further instructions for enforcement of the Law of August 28, 1830 and requires the examination of inventions after granting a patent.
f) Law # 3.129/82: Privileges Act, appended by Decree # 8.820, December 30, 1882, aimed primarily at adapting Brazilian legislation to the resolutions of the Paris International Congress on Industrial Property in 1880, as well as conclusions from previous congresses convened in Vienna in 1873 and Paris in 1878.

g) Decree # 16.264/23: regulates Industrial Property, creates the General Industrial Property Directorate, and amends previous legislation.

h) Decree # 24.507/34: appends Industrial Property legislation and introduces provisions pertaining to industrial designs and models, trade names, and unfair competition.

i) Decree/Law # 7.903/45: passes Industrial Property Code, consolidating Industrial Property legislation. Relevant changes in this legislation included the novelty concept, exclusion of patentability for foodstuffs or medicines inventions obtained by chemical means or processes.

j) Decree/Law # 254/67: creates new Industrial Property Code, focusing on exclusion of the utility model.

k) Decree/Law # 1.005/69: establishes new Industrial Property Code, which adds foods, chemicals, and pharmaceutical products, materials and medicines to the list of non-patentable materials.

l) Law # 5.772/71: establishes new Industrial Property Code, maintaining patentability exclusion for foods, chemicals, pharmaceutical products, materials, mixtures, and medicines of any kind, as well as the processes for obtaining or modifying them.

m) Law # 9.279/96: establishes new Industrial Property Code, resulting in relevant changes to the previous Code, highlighting patentability of products and processes from the pharmaceutical and biotechnology industries, introducing the *pipeline* mechanism. This Law was developed in order for Brazilian Industrial property legislation to comply with the TRIPS Agreement

n) Law # 10.196/01: Modifies and adds clauses to Law# n° 9.279/96, including the Bolar exception flexibility (article 43), and establishes patent pending approval to the National Agency of Health Surveillance (ANVISA) to expedite patents for products and pharmaceutical processes.

o) Decree # 3.201/99 establishes grounds for issuing compulsory licenses in cases of public interest and national emergencies

p) Law #10.603/02 – establishes protection of undisclosed data submitted by the pharmaceutical industry to national regulatory authorities for obtaining market approval for veterinary pharmaceutical products, fertilizers as well as agrotoxics and their components.

q) Decree # 4.830/2003 modifies articles 10, 20, 50, 90 and 100 of Decree 3.201/99.

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Chapter 9

Pharmaceutical Patent Protection in Brazil: who is benefiting?

Maria Auxiliadora Oliveira, Jorge A. Z. Bermudez, Ruth Epsztejn, Gabriela Costa Chaves, Rogério Luiz Ferreira & Maria Telma Oliveira

The international system of intellectual property was implemented in 1883, when the Paris Declaration was signed. This system went through many revisions and adaptations to meet the trade demands of each period.

Until the 1950s no major focus was placed upon property rights for pharmaceutical products. In the beginning of the 1950s, the pharmaceutical industry came to play an important role in the economy. Consolidation and growth of transnational companies intensified, largely due to technical dominance of chemical synthesis, which occurred in the previous decade. During the Golden Age of the pharmaceutical industry, between 1950 and 1970, thousands of new medicines were developed. At the end of this period the theme of patents for pharmaceutical products gained much visibility. This happened because countries that had invested in technological development and expansion of their national industries needed to protect their production from internal and external competition. Thus, these countries, in addition to implementing national systems of patent protection also began to demand that other countries with less technological capacity should do so as well. Their justification stemmed from the belief that countries which did not protect patents would subsequently promote anticompetitive practices and market copies of their innovator products. It became evident that patents were a powerful instrument of market control, because they guaranteed the exclusive rights of commercialization and also limited possibilities for competition. This system thereby ful filled the economic interests of patent holders to appropriate their scientific knowledge and invention technology.

This scenario gave rise to transnational industry interests, headquartered in developed countries, summarized by the following arguments:

(1) patents are a necessary incentive for the technological innovation of drugs; this system has generated important health goods on a global scale;

(2) patents guarantee financial return for the large investments in research and development made by the private sector, which has stimulated development in science and technology;

(3) patents accelerate the transfer of technology from the developed world to the developing world, ensuring a relatively equal distribution of gains from this policy change (Bale, 2002; Branstetter *et al.*,2002, IFPMA & RDPAC, 2003; IFPMA, 2003).

Developing countries, on the other hand, may not benefit from this system. Penrose (*apud* Tachinardi, 1993) questions the benefits obtained for the importing country, which concedes property rights to foreign inventors. According to the author, the monopoly conferred by a patent produces three effects: (1) increase in price of the imported product, (2) increase in the rate of innovation for the exporting country, and (3) increase in the availability of technological information of patented inventions. Penrose also analyzes the cost/benefit ratio of issuing patents to foreigners, and concludes that the costs are high and that the benefits are dubious for the majority of developing countries. The costs of patented products are assumed by the importers and the benefits revert almost exclusively to the exporter, "an international patent regime attends more to the interests of large industrial groups, established in industrialized countries, which have ample industrial infrastructure and also a high rate of innovation. For lesser and non industrialized countries the gains are null (*ibid.*:79)."

Different opinions were expressed among the actors involved in the discussion about patents and the pharmaceutical industry during the Uruguay Round, which ended in April 1994. In this arena, the pharmaceutical industry finally was able to impose its longstanding wish to grant patent protection for its products in all WTO Member States, as established in the TRIPS Agreement.

The negotiations about intellectual property within this Round were initiated by developed country governments, particularly those who harbor headquarters of large transnational pharmaceutical companies. These

governments were able to include in the TRIPS Agreement stringent patent protection standards to be adopted by all WTO Members. These standards were, notwithstanding, stricter than the ones originally recognized by their own countries at the time.

TRIPS harmonized IP standards worldwide. It also requires patent protection in all technological fields including medicines. One criticism of this system is that it does not allow WTO Member countries to adopt the best possible patent protection regime in order to facilitate social and economic development (Gontijo, 2003; as stated in chapter 1).

This chapter analyzes some aspects of the TRIPS Agreement implementation and the recent changes in Brazilian intellectual property legislation concerning the pharmaceutical industry. The analysis is based on the number and type of patent claims filed by the pharmaceutical industry and technology transfer contracts registered in the National Institute for Industrial Property (INPI), the Brazilian government agency in charge of Intellectual Property. We reviewed the first five years of the new Industrial Property Law, enacted on May 14, 1996 (Brasil, 1996). The study aimed to answer the following questions:

1. Did the number of patent claims in the pharmaceutical industry increase?

2. From what countries are all of the patent claims coming from?

3. What is the percentage of patent claims filed by Brazilian institutions or individuals?

4. Did the number of technology transfer contracts in the pharmaceutical industry increase?

5. Can the kind of technology transferred potentially improve the technological capabilities in the local pharmaceutical industry?

Methodology

In order to better analyze the implications of recent changes in Brazilian patent legislation for the local pharmaceutical industry in particular, patent claims records were divided according to the nature of production, classifying them initially as chemical or biotechnological[1] claims.

According to the technological level, biotechnology may be classified as traditional or new. This distinction arose with the discovery and development of recombinant DNA technology in 1974, providing the basis for new biotechnology and substantially changing the nature of this science. In this work we adopt this same classification of biotechnology patents.

We also classified patent claims in the Brazilian pharmaceutical industry from August 1992 to December 2002 by number and country of origin. Despite the fact that the Industrial Property Act, in force before the current one, did not allow patenting in the pharmaceutical industry, patent claims were nevertheless filed at the National Institute for Industrial Property (INPI).

Data was gathered over a ten-year period from 1992 to 2002. Note that a patent claim may include more than one individual or corporation as filers. Consequently, the number of countries of origin is always greater than or equal to the number of claims.

To demarcate the fields under study, we adopted the following definitions:

(a) pharmaceutical: includes all pharmaceutical products of chemical (synthetic) or natural origin, technically prepared or obtained and used prophylaxis, diagnosis or cure of medical of veterinary conditions, except:

- diet products for persons with special physiological needs, weight-loss products, and contraceptives;
- cosmetics in general (except products for dermatological purposes) shampoos, herbicides, insecticides, fungicides, and fertilizers.

(b) Chemical entities with pharmacological and therapeutic activity.

(c) Biotechnology: includes all primary and secondary products of traditional or modern biotechnological origin.

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[1] Biotechnology is defined as any technology that uses living beings or functional parts isolated from them in the production of goods and services.

To better identify patent claims in the pharmaceutical industry meetings were held with the technical staff of the National Institute for Industrial Property (INPI), using the International Classification of Patents, 6th Edition, 1994. The relevant sub-classes were defined for the pharmaceutical industry: chemical, traditional biotechnology, and new biotechnology.

The data presented are from patent applications filed with the INPI, and published in the Industrial Property Magazine (RPI) by the same agency.

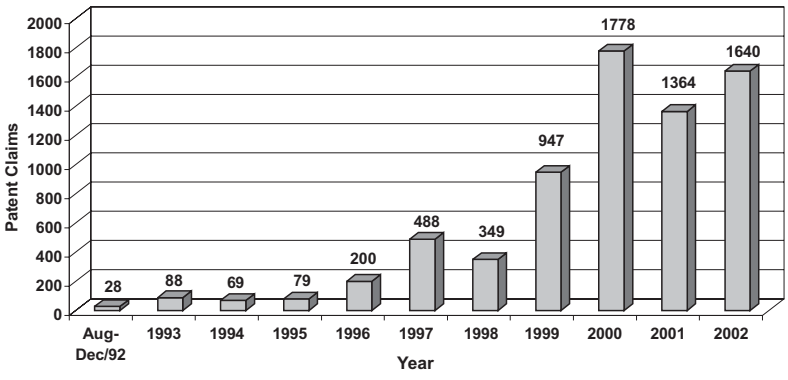
Technology transfer (TT) contracts in the Brazilian pharmaceutical industry were analyzed in order to infer whether new IPR legislation complying with the TRIPS Agreement contributed towards expanding local R&D in this field. This analysis evaluated these contracts quantitatively and qualitatively from 1992 to 2001.

Results

Annual Number of Patent Claims Filed

Figure 1 shows the trend in the number of chemical patent claims filed by the pharmaceutical industry from August 1992 to December 2002, emphasizing that on May 14, 1996, the Industrial Property Code was approved under Act # 9.279/96 and enforced in 1997.

FIGURE 1: Chemical Patent Claims filed by the Pharmaceutical Industry, Brazil, Aug. 1992 to Dec. 2002



Source: Elaborated from patent file data published in RPI/INPI.

From August 1992 to December 2002, a total of 7,030 chemical product patent claims were filed by the pharmaceutical industry. In 1996 and 1997, claims more than doubled as compared to the previous years. However, this same increase was not observed in 1998. In the following years, particularly in 1999 and 2000, the number of claims increased sharply. The trend continued(more than 1,000) in 2001 and 2002.

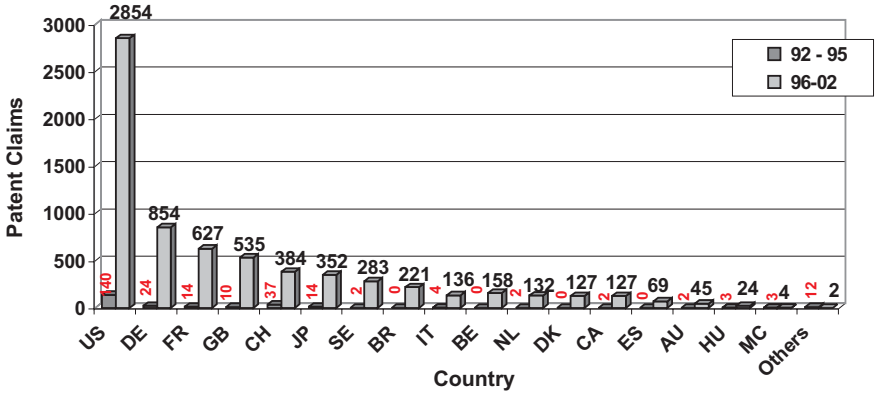
The number of claims filed in 1996 was quite large due to the fact that although the new Industrial Property Act was only passed in May of that year, the Federal government had been discussing changes in the legislation since 1990, hence generating expectations in early 1996 that the new Act would soon enter into force.

The total number of claims filed from August 1992 to December 1995 was 264, only 32% more than the total for the year 1996 alone (200 claims). A total of 488 claims were filed in 1997, an increase of over 144%. In the year 1998, 349 claims were filed, a slight decrease of 28.5%. In 1999, the number of patent claims almost tripled (947) comparing to 1998, reporting an increase of 271%. In the year 2000, the number of patent claims filed had reached 1778, 187% higher than the previous year. In 2001 and 2002 the number of patent claims filed were more than 1,300.

Patent Claims Filed by Country of Origin

The total study period, from August 1992 to December 2002, was split into two periods in order to detect any change in behavior by the countries with patent claims in the pharmaceutical industry before and after the new Brazilian Industrial Property Code entered into force.

FIGURE 2: Chemical Patent Claims in the Pharmaceutical Industry by Country of Origin, Brazil, Periods Aug/1992-Dec/95 and Jan/96 to Dec/2002



Source: Elaborated from patent file data published in RPI/INPI.

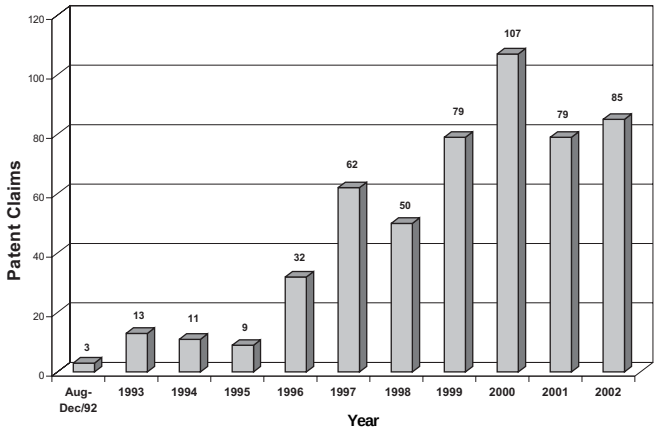
From August 1992 to December 1995, the country with the most patent claims in the pharmaceutical sector in Brazil was the United States (US), with 140 claims filed, or 52% of the total. This number was nearly four times that of the second country, Switzerland (CH), which filed 37 claims. During this period, there was no record of Brazil (BR) having filed for a patent pertaining to a chemical product in the country.

Figure 2 analyzes the chemical product claims filed from 1996 to 2002 by country of origin in the pharmaceutical industry in Brazil; the total number of claims was 6,934. The United States (US) continued to lead with 2,854, with over twenty times the number of applications it filed from August 1992 to December 1995. On the other hand, the United States' proportional share of all claims during this period dropped to 41%, which reflects the fact that other countries increased their claims for patent protection in Brazil during this period.

Beginning in 1996, many countries stepped up their patent applications in this field. Examples include Germany(DE), which increased its share from 8.9% to 12.2%, and Great Britain (GB), from 3.7% to 7.7%. Other countries began filing claims, like Canada (CA) and Sweden (SE), with 127 and 283 claims, respectively.

Brazil only filed 221 claims, a very small number. Since 1996, Brazil's share has only been 3.1% of the industry's total.

FIGURE 3: Patent Claims Filed for Traditional Biotechnology in the Pharmaceutical Industry, Brazil, Period from Aug/92 to Dec/2002

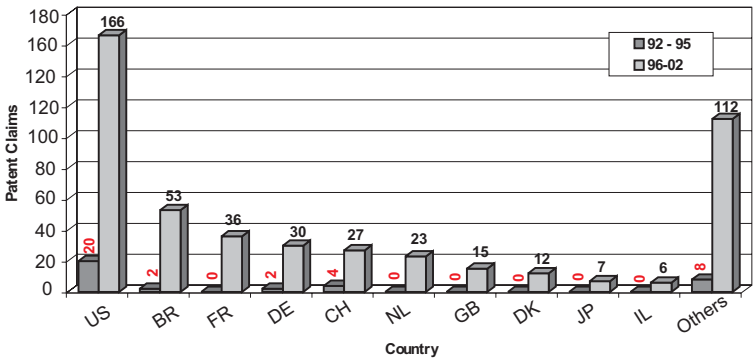


Source: Elaborated from patent file data published in RPI/INPI.

Despite the few claims filed for traditional biotechnology in the pharmaceutical sector (as compared to chemical claims), totaling 530 applications, from 1997 onwards, there is an increase in the number of claims filed, with a peak of 107 in the year 2000.

Figure 4 shows the trend in patent claims filed for traditional biotechnology in the pharmaceutical industry by country of origin in the period before and after the change in Brazil's Industrial Property legislation.

FIGURE 4: Patent Claims Filed for Traditional Biotecnology in the Pharmaceutical Industry by Country of Origin Brazil, Periods 1992-1995 and 1996-2002



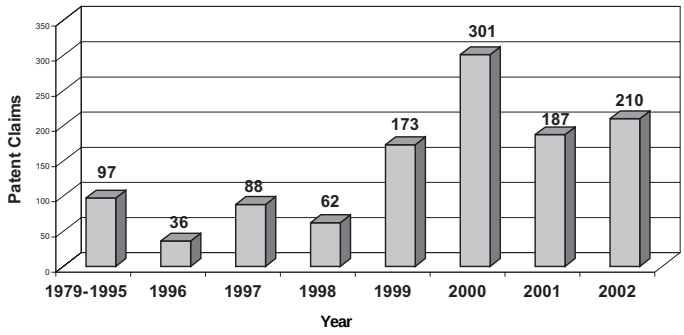
Source: Elaborated from patent file data published in RPI/INPI.

From August 1992 to December 1995, the United States (US) filed most patent claims, 20 out of 36, thus accounting for 56% of the total. Brazil filed only 2 claims, accounting for 6% of the total.

The country with the most claims for traditional biotechnology in the pharmaceutical industry after the new Act was passed was the United States (US), with 166 claims, or 34% of the total. Brazil (BR) was second, with 53 claims, or 10.8% of the total.

Figure 5 shows the quantitative trend in claims pertaining to new biotechnology in the pharmaceutical industry.

FIGURE 5: Patent Claims Filed for New Biotechnology in the Pharmaceutical Industry, Brazil, 1979 to 2002.

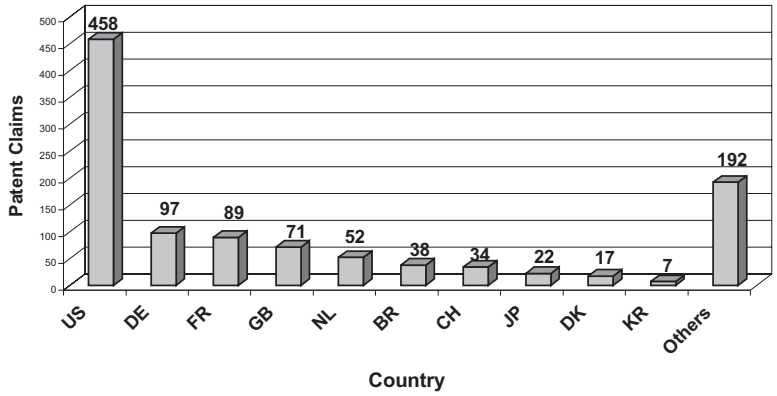


Source: Elaborated from patent file data published in RPI/INPI.

The amount of claims filed from 1997 onward has increased, with a peak of 301 claims in the year 2000.

Country-of-origin data pertaining to claims for new biotechnology in the pharmaceutical industry from 1996 to 1998 are shown in Figure 6.

FIGURE 6: Patent Claims Filed for New Biotechnology in the Pharmaceutical Industry, by Country of Origin, Brazil,1996-2002



Source: Elaborated from patent file data published in RPI/INPI.

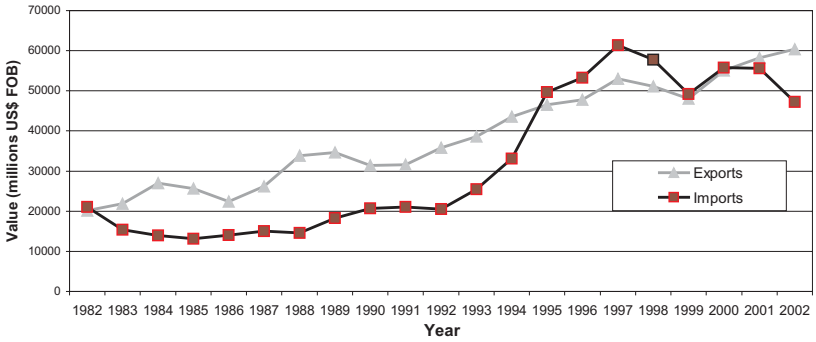
The country with the most claims was the United States (US), with 458 patent applications, or 42% of the 1077 claims filed. Second, came Germany (DE) with 97 applications. Brazil (BR) was the sixth, with a total of 38 claims filed, or 3.5% of the total.

Patent Protection and Balance of Trade in Brazil

In analyzing Brazil's total balance of trade (Figure 7), 1982 showed a negative balance. However, the balance was positive from 1983 to1994, and became negative again from 1995 to 1998. Note that in 1998 the balance was 21% below that of 1997. Imports declined 6% in 1998 compared to 1997, and although exports also dropped, the decline was only 3% compared to the previous year.

In the following three years (1999-2001) there has been a balance between imports and exports, and in the year 2002, imports were 22% lower than total exports.

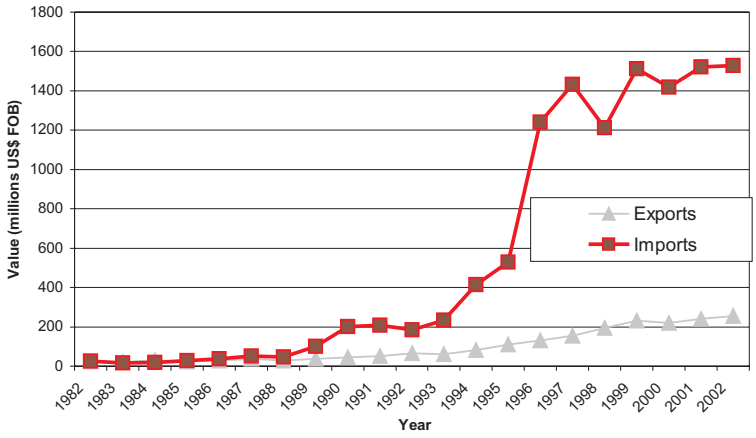
FIGURE 7: Brazil's Total Balance of Trade, 1982 to 2002



Source: Anuário Estatístico do Brasil - FIBGE and SECEX/MDIC

Figure 8 shows the trend in imports and exports of pharmaceutical products in monetary values, for the period from 1982 to 2002.

FIGURE 8: Brazil's Balance of Trade in the Pharmaceutical Industry, from 1982 to 2002



Source: Anuário Estatístico do Brasil - FIBGE and SECEX/MDIC

Comparing imports of pharmaceutical products with Brazil's total imports for the period 1982-2002, Brazil's total imports increased by 224%, while those for pharmaceutical products grew by 6,112%. Exports of pharmaceutical products during the same period grew by 1,104%, while total Brazilian exports increased by only 299,4%.

Over the course of this period, the balance for pharmaceutical products was consistently negative, except for the years 1983 and 1984. The total number of pharmaceutical products imported by Brazil grew sharply, except for the year 1998, when there was a slight decline. The share of exports stayed at modest levels, while in the year 1998 there was a slight increase as compared to the previous year; nevertheless, one must keep in mind that total Brazilian exports were lower in 1998 than in 1997 (figure 7).

Technology Transfer Contracts of the Brazilian Pharmaceutical Industry

The Brazilian Patent Act # 9.279/96 states in Art. 211 – that "INPI will register contracts for technology transfers, franchise contracts and other similar arrangements that will effect third parties." Summaries of the registered contracts are published in the Industrial Property Magazine of INPI under the following categories: license for brand name use (BNU); franchising (FRA); technology supply (TS); patent exploitation (PE); cost sharing of research and development (R&D); technical assistance services (TAS).

Table 1 shows the distribution of Technology Transfer Contracts in the pharmaceutical industry in Brazil during the period from 1992 to 2001, by type of contract.

TABLE 1: Technology Transfer Contracts in the Pharmaceutical Industry, Brazil, 1992 – 2001

TYPE/ YEAR	BNU	FRA	TS	PE	R&D	TAS	Other	TOTAL	% BNU	% TAS	% TS
1992	104	-	-	-	-	2	4	110	94.55	1.81	
1993	90	-	-	1	-	7	-	98	91 84	7.14	
1994	66	-	4	-	-	8	1	79	83.54	10.13	5.06
1995	50	-	-	1	-	8	3	62	80.65	12.9	
1996	49	-	3	1	2	11	1	67	73.13	16.42	4.47
1997	39	-	1	-	3	9	-	52	75	17.31	1.92
1998	14	3	5	-	-	11	-	33	42.42	33.33	15.15
1999	34	3	7	2	-	10	-	56	60.71	17.86	12.5
2000	22	2	6	1	-	15	-	46	47.83	32.61	13.04
2001	16	-	2	2	-	14	-	34	47.06	41.18	5.88

Source: Elaborated from data published in RPI/INPI

Type of Contract: BNU – License for Brand Name Use- FRA – Franchising- TS – Technology Supply- PE – Patent Exploitation- R&D – Research and Development- TAS –Technical Assistance Services

A considerable decrease (69.1%) was observed in the total number of technology transfer contracts in the pharmaceutical industry of Brazil during the time period studied. The total number of registered contracts in INPI went from 110 in 1992 to 34 in 2001, continuing to drop after law 9276/96 entered into force. This result contradicts the argument that strengthening IP systems accelerates technology transfer from developed to developing countries.

Second, it is important to highlight that the majority of Technology Transfer contracts were for Brand Name Use and Technical Assistance. The figures for contracts on Technology Supply (around 5%) and on cost sharing R&D (almost 0%) indicate that the type of technology being transferred does not contribute to the improvement and technological development of the local pharmaceutical industry.

The data shown in Figure 8 corroborates this statement, because there have been large increases in pharmaceutical industry imports without similar increases in exports; this indicates a high level of technological dependence in this sector.

Conclusions

Since the adoption of the current Brazilian Industrial property law in May 1996, there has been an important trend of increased growth in the number of patent claims filed by the pharmaceutical industry in Brazil. When considering the country of origin for patent claims, developed countries are responsible for more than 95% of the total. This may indicate that countries, such as Brazil, with less R&D investment and infrastructure capacity are unable to take further advantage of the benefits conferred by patents. Additionally, the figures presented show a considerable increase in importation by the pharmaceutical industry, providing evidence of the growing trend in Brazil towards external technological dependency. In the context of the TRIPS Agreement, this type of dependency may increase since the pharmaceutical industry has concentrated research, development and production in developed countries.

Thus, when Brazil grants a patent to the pharmaceutical industry, it is in fact protecting foreign company patent holders from internal and external competition. The lack of local production of the patented product or process

means that Brazil loses the opportunity to use and to learn from invention disclosure, which happens when a patent is granted. Analyses of technology transfer contracts corroborate this unfavorable scientific and technological development scenario.

In conclusion, all of the parameters analyzed in this chapter have made it clear that the greatest beneficiaries from the recent changes in Brazilian industrial property legislation are not Brazilian companies or institutions, but rather, transnational corporations, who maintain hegemony of the Brazilian market. Therefore, efforts are needed to establish alternatives and strategies in order to effectively implement public policies committed to Brazilian technological development.

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