

**Reforming pharmaceutical regulation:  
a case study of generic drugs in Brazil**

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## **Declaration**

I hereby declare that this thesis is my own work and effort and that it has not been submitted anywhere for any award. Where other sources of information have been used, they have been acknowledged.

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## Abstract

Brazil is renowned worldwide for its remarkable reforms in pharmaceutical regulation, which have enhanced access to essential medicines while lowering drug costs. As part of these reforms, the *Generic Drug Act* was introduced in 1999. This policy mandates that pharmaceutical products that are no longer protected by a patent must be interchangeable with an innovator (reference) drug. This thesis examines how and why Brazil promoted this large-scale regulatory policy. The literature on pharmaceutical policy often invokes international guidelines that inspire countries to reformulate their regulatory regimes or argues that regulations emerge in order to serve the interests of powerful interest groups. In contrast, this thesis examines how changes in the regulatory environment affect actors' policy preferences. It argues that as actors adapt and respond to new regulatory environments, they also push the policy path further along the way.

This historical qualitative case study relies on in-depth interviews and documentary research to trace the policy process of generic drug regulation in Brazil. It finds that Brazil's generic drug reform can be attributed to a convergence of the evolution of pharmaceutical regulation, unexpected events (AIDS epidemic and scandal of fake medicines) and political activity of the Minister of Health. In turn, this study demonstrates that the new regulatory development altered the preferences of local pharmaceutical firms, who now support and uphold a policy they once opposed because of the high costs associated with adapting their industrial plants and processes. The regulation of generic drugs has also culminated in other unintended consequences. Public pharmaceutical factories were still unable to fully adjust to the new regulatory environment and patient groups slowly became aware of these limitations. Paradoxically, the generic drug regulation introduced in the name of patients and opposed by local pharmaceutical firms, is today opposed by important patient advocacy groups but solidified by the strong support of local and multinational pharmaceutical firms.

These findings suggest although pharmaceutical firms strongly support the generic drug regulation today; they did not control the policy process that created it. Although Brazil's norms resemble international guidelines, they were developed locally. Brazil's case demonstrates that evolution of domestic political institutions were the most important determinant of the timing and direction of the regulatory policy. Thus, this thesis concludes that the state still matters for pharmaceutical regulation and that pharmaceutical regulation is only partially influenced by non-state actors.

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## Table of Contents

<b>Declaration</b> .....	<b>2</b>
<b>Abstract</b> .....	<b>3</b>
<b>Acknowledgements</b> .....	<b>4</b>
<b>Table of Contents</b> .....	<b>6</b>
<b>List of Tables</b> .....	<b>8</b>
<b>List of Figures</b> .....	<b>8</b>
<b>List of Abbreviations</b> .....	<b>9</b>
<b>Introduction</b> .....	<b>11</b>
Background .....	16
What is a generic drug policy?.....	16
Health system and pharmaceutical reforms in Brazil .....	23
Thesis outline .....	27
<b>1. Contextualising generic drug regulation</b> .....	<b>29</b>
Preceding studies on generic drug regulation .....	31
Economic studies .....	31
“Perception” literature .....	33
Generic drug regulation from a political perspective.....	35
Global health and the diffusion of international guidelines.....	36
Positive theories of regulation .....	42
The Brazilian context.....	48
Lessons from the literature review and study aim .....	53
<b>2. Theoretical framework: preference formation, policy outcome and the study of generic drug regulatory process</b> .....	<b>57</b>
Policy shapes politics .....	57
Studying rationality: intentional vs. constructed action.....	61
Understanding preference formation .....	68
Multiple effects and multiple interests.....	68
Prevalence of uncertainty.....	70
Role of interpretation to preference formation .....	71
Preference formation.....	72
The role of temporality in the process of preference formation .....	74
Conclusion – the argument in brief.....	77
<b>3. Methodology</b> .....	<b>81</b>
Research Design.....	81
Case study and process tracing approach.....	82
Studying the process of generic drug regulation in Brazil.....	88
Methods.....	93
Documentary research.....	93
Semi-structured interviews .....	97
Quantitative data .....	101
Data Analysis .....	102
Ethical Issues .....	106
Institutional support & fieldwork funding .....	107
Conclusion .....	108

<b>4. The generic drug reform in Brazil.....</b>	<b>109</b>
Background: local production of medicines .....	109
Institutional antecedents.....	112
Early attempts to introduce Generic drugs.....	113
Patent system reform: Bill 824/1991 and Law 9279/1996 .....	118
The HIV/AIDS activism .....	125
Reform period: political activism and uncertainty.....	130
Reform phase 1: Parliamentary negotiations and the Generic Drug Act.....	134
Reform phase 2: Governmental activism to implement generic drugs.....	141
Conclusion .....	155
<b>5. Assessing the generic drug regulatory process in the 2000s: governmental intervention, market demand and local pharmaceutical industries.....</b>	<b>158</b>
Background: economic outcomes .....	159
Government advocacy and market demand .....	162
Governmental intervention .....	162
Market demand .....	169
Local pharmaceutical manufacturers .....	172
Reorganising collective action to accommodate the new interests.....	175
Adjusting similar drugs and reinforcing the path.....	177
Framing the generic drugs: access to safe and efficient medicines .....	181
Using comparative advantage: commercial acumen.....	185
Multiple interests: the intellectual property debate.....	188
Pipeline mechanism .....	191
TRIPS Plus agenda: polymorphs and second use .....	194
Procedure to register pharmaceutical patents in Brazil.....	198
Conclusion .....	201
<b>6. Public production of medicines and HIV/AIDS activists: new actors in the generic drug regulatory process.....</b>	<b>205</b>
Public pharmaceutical industries .....	206
HIV/AIDS Activists.....	214
Regulation of antiretroviral generic drugs .....	218
Multiple interests: the intellectual property debate.....	223
Pipeline mechanism .....	224
TRIPS Plus agenda: polymorphs and second use .....	226
Procedure to register pharmaceutical patents in Brazil.....	228
Additional agendas.....	228
Conclusion .....	234
<b>Conclusion.....</b>	<b>237</b>
The research problem revisited and empirical findings.....	237
Theoretical implications.....	245
Global health implications .....	251
Limits of the study and direction for further research .....	253
<b>References .....</b>	<b>256</b>
<b>Annex 1. Interview protocol.....</b>	<b>294</b>
<b>Annex 2. List of Interviewees .....</b>	<b>297</b>
<b>Annex 3. Consent form model .....</b>	<b>299</b>
<b>Annex 4. Evolution of generic drug sector in Brazil .....</b>	<b>301</b>
<b>Annex 5. Public-private partnerships enable 24 drugs to be produced nationally.....</b>	<b>303</b>

## List of Tables

Table 1. Types of pharmaceutical products in selected Latin American countries ...	22
Table 2. Ranking of pharm industries in Brazil (US\$), 1999 and 2005-2009 .....	53
Table 3. Research design rationale for assessing the reform period.....	90
Table 4. Research design rationale for assessing policy development .....	92
Table 5. Summary of documentary research .....	96
Table 6. Groups of informants according to the number of interviewees.....	99
Table 7. Events attended during field research.....	101
Table 8. Events discussed in Chapter 4 .....	104
Table 9. Ranking of pharma. industries in Brazil (US\$), 1999 and 2005-2009 .....	174
Table 10. Ministry of Health expenditure (US\$) on ARV purchases per pharma. Supplier. Brazil, 1996-2006.....	211
Table 11. Index of generic drugs and total pharma. market (vol). Brazil, 2003-9...	302
Table 12. Index of generic drugs and total pharma. market (R\$). Brazil, 2003-9...	302

## List of Figures

Figure 1. Policy effect and preference formation .....	73
Figure 2. Illustration of Chapter 5 and 6 rationales .....	106
Figure 3. Newspaper images of Microvlar incident.....	133
Figure 4. Illegitimate advertisements of generic medicines in July 1999.....	143
Figure 5. Illegitimate advertisements of generic medicines in July 1999.....	144
Figure 6. Generic drug label according to Brazilian regulatory rules.....	155
Figure 7. Jose Serra's Presidential election campaign, 2002 and 2010 .....	163
Figure 8. Market share (vol) of generic pharma. producers in Brazil in 2007.....	174
Figure 9. Evolution of generic drug market in sales (US\$ 000). Brazil, 2000-2008	301
Figure 10. Evolution of generic drug market in sales (vol). Brazil, 2000 to 2008 ..	301
Figure 11. Type of private sector investments to generic drug manufacturing. Brazil, 1999-2004 .....	302



## List of Abbreviations

ABIA	Brazilian Interdisciplinary AIDS Association
ABIFARMA	Brazilian Association of Pharmaceutical Industries
ABIFINA	Brazilian Association of the Fine Chemistry, Biotechnology and its Specialties Industries
AIDS	Acquire immunodeficiency syndrome
ALANAC	Brazilian Association of National Pharmaceutical Industries
ALFOB	Brazilian National Association of Public Laboratories
ANVISA	Brazilian Regulatory Health Surveillance Agency
API	Active Pharmaceutical Ingredient
ARV	Antiretroviral
BNN	Brazilian Non-proprietary Name
CL	Compulsory license
EU	European Union
FDA	Food and Drug Administration
FEBRAFARMA	Brazilian Federation of Pharmaceutical Industries
FURP	Foundation for Popular Remedy
GTPI	Working-Group on Intellectual Property
HAART	Highly Active Antiretroviral Therapy
HAI	Health Action International
HIV	Human immunodeficiency virus
INN	International Non-proprietary Name
IP	Intellectual property
NGO	Non-governmental Organization
PAHO	Pan American Health Organization
PIC	Parliamentary Investigative Commission
PPP	Public and private partnership
PSDB	Brazilian Social Democracy Party
PT	Workers Party
SINDUSFARMA	Sao Paulo Syndicate of Pharmaceutical Industries

SUS	Unified Health System
TRIPS	Trade-related Aspects of Intellectual Property Agreement
WHO	World Health Organization
WTO	World Trade Organization

## Introduction

Brazil is renowned worldwide for its remarkable reforms in pharmaceutical regulation, which have enhanced access to essential medicines while lowering drug costs (Dias and Romano-Lieber 2006; Piovesan and Labra 2007; Nunn 2008). As part of these reforms, the Brazilian Congress, with the support of the Ministry of Health, approved the Generic Drug Act in 1999. A generic drug is a pharmaceutical product that is no longer protected by a patent, and is interchangeable with an innovator drug (World Health Organization 2001). Normatively, a generic drug policy is an intervention to foster market competition, which would prompt price declines and increase access to safe and affordable medicines (*ibid*). In Brazil, over 80% of drug expenses are paid for by patients themselves (Cohen 2000), resulting in pricing being a core determinant of access to medicines. Studies suggest that generic drugs enter the market with an average price of 40% lower than its patent version and this difference has increased over time, making medicines more affordable to the Brazilian population and governmental programmes (Vieira and Zucchi 2006).

Other research suggests that the Minister of Health and presidential hopeful, Jose Serra, promoted the reform as a response to a crisis in the pharmaceutical sector triggered by a scandal involving fake birth control pills (Dias 2003; Franca 2004; Dias and Romano-Lieber 2006). However, because these studies focus only on the critical period of reform, little is known about the institutional antecedents and policy process that channeled this entrepreneur activity. Additionally, although much has been said about the remarkable impact of Brazil's generic drug competition on the market and price structure (Abreu 2004; Nishijima 2008; Quental et al. 2008; Rosenberg et al. 2008; Rosenberg 2009), the process that influenced the adoption of this large-scale regulatory reform has not been well explored in the literature. This is particularly intriguing because a regulatory shift in the pharmaceutical sector requires the participation of a number of stakeholders and interest groups in the policy process. This thesis therefore examines how and why Brazil adopted a generic drug policy, examining the regulatory policy process from its genesis in 1990 to the

most recent developments in 2009. It appears that no study has approached the generic drug regulation in Brazil from this perspective.

There are two prominent analytical explanations as to why countries promote large-scale pharmaceutical policies. The first refers to the diffusion of international guidelines that inspire other countries to reformulate their regulatory regimes (cf. Carpenter 2010). Other scholars argue that regulations emerge in order to serve the interests of powerful interest groups, who are usually small and homogeneous. Apparently, these explanations are ill-equipped to understand Brazil's case. If the World Health Organization (WHO) had been broadcasting generic drug policies since the 1980s, why did the idea not catch on in Brazil earlier? Why did previous studies of Brazil's case focus on the political entrepreneurship of the Minister of Health, rather than powerful firms or patient advocacy as a key condition to the reform? Additionally, if the political entrepreneur (who has been credited as the main protagonist of the generic drug reform) is no longer in a position to influence decision making in the pharmaceutical sector, how can we explain the development of generic drug regulation?

To answer these questions, this thesis takes an alternative approach to the mainstream literature on pharmaceutical regulation. It suggests that a more promising analytical frame is to observe how policy legacies shape the preferences of actors; that is, interest groups' preferences are constructed within the regulatory policy process. Thus, to elucidate the regulatory process of generic drugs in Brazil, this study examines the reform from its antecedent periods to the policy returns that follow this restructuring. This historical frame provides elements in which to assess the actors participating in the generic drug policy process, to understand the content of their demands, and how they pursue these claims. In turn, it assesses both policy change and sustainability. On a more abstract level, this study analyses two separate but related social phenomena. The first is policy outcome; this argues that policy decisions taken in critical periods of reform might become path dependent, that is, once a policy path is chosen, actors adapt to the existing policy in ways that push them further along that trajectory (cf. Pierson 2004). The second is preference

formation; this argues that it is in the interaction with the policy process that actors define what they want and how to portray their demands - in other words, their preferences are socially constructed (Hall 2005; Woll 2008). These two complementary analytical tools help to contextualise the circumstances by which Brazil decided to implement a generic drug policy, whilst assessing the effects on the participants involved with the making of pharmaceutical regulation.

### **Research methods and empirical data**

This thesis is based on rich empirical qualitative and quantitative data and historical narrative that traces the process of generic drug policy in Brazil. The qualitative scope included 57 in-depth interviews with HIV/AIDS and diabetes activists, business representatives, experts on pharmaceutical regulation, government officials and politicians. It also included the 2002 and 2010 presidential candidate Jose Serra, who was responsible for championing the reform in 1999, and four former Congressmen who proposed generic drug bills in the past. All interviewees were selected based either on their engagement with the policy process to some extent or that they had some expertise on this topic. This thesis is also based on hundreds of government documents and newspaper articles, dating from the late 1980s to 2010. The quantitative component, which included information about economic outcomes of the generic drug regulation, is based on market intelligence data (e.g. Intercontinental Marketing Services – IMS Health), academic research and business association analysis. It also included historical spending on pharmaceutical assistance programmes that was informed by the Brazilian Ministry of Health.

### **Key findings**

This study concludes that Brazil's generic drug reform can be attributed to the contingent convergence of institutional evolution (e.g. enactment of an Intellectual Property Law in 1996) and the Minister of Health's political activity. This reform aimed to improve the regulatory standards of off-patent pharmaceutical products commercialised in the country, foster market competition and increase patient access to safe and affordable medicines. This study demonstrates that regulatory development has altered the preferences of local pharmaceutical firms, who support

and uphold a policy that they were once opposed to, given the high costs to adapt their industrial plants and processes. However, in the face of a crisis in the sector, these firms decided to reformulate their preferences and demands, adjusting to the new regulatory environment. They supported preference in favour of generic drug regulation during the 2000s, in spite of the few governmental investments in mass media campaigns to promote these products among the population and the reported suspicious of consumers (health professionals and patients). Had the firms not adapted, pharmaceutical regulation in Brazil may not have changed much since 1999, and there would still be competition between patented and similar products.

In addition, this thesis found that the regulation of generic drugs has also produced unintended consequences for public pharmaceutical factories, a core pillar of Brazil's celebrated HIV/AIDS response, as they are still unable to fully adjust to the new regulatory environment. Brazil has produced antiretroviral medicines that do not fit the criteria for generic drug products for more than two decades in public factories for the National AIDS Program. The recent engagement of AIDS groups in the regulatory process highlights how actors' preferences were slowly constructed within the regulatory process, but also underscores the limitations of changing the norms once they become path dependent. Because there is a consensus among suppliers on the regulatory norm enacted in 1999, it has been difficult for these groups to challenge the current state of affairs of generic drug regulation in Brazil. Paradoxically, the generic drug regulation, introduced in the name of patients and opposed by local pharmaceutical firms, is today opposed by important patient advocacy groups but locked in by the strong support of local and multinational pharmaceutical firms.

### **Implications of this study**

The study of generic drug regulation is a field largely concerned with the economic effects of market intervention on the price of medicines, the structure of competition and also with the behaviour of health professionals and consumers in demanding these products (cf. Grabowski and Vernon 1992; Beecroft 2007; Grabowski and Kyle 2007; Losifescu et al. 2008). Despite the clear political salience of pharmaceutical policies, the politics of generic drug regulation goes unnoticed and unresearched .

Although this single case study cannot be generalised in terms of causal inference, the intention here is to provide a theoretical and practical contribution. From a practical point of view, pharmaceutical policy has far-reaching consequences for public health; for instance, it can limit or foster the supply of affordable drugs, or poorly regulated products can cause abortions, malformation or even death. In this sense, important questions to be considered are whether generic drugs should go through the same approval process as innovator medicines in order to be considered a good quality product, or whether pharmaceutical products that are not interchangeable with an innovator drug should be considered substandard. The dilemma behind these questions goes beyond the scientific debates and mobilises different interests and groups of society with a stake in pharmaceutical regulation. Thus, analysing those factors that influence the formulation and development of generic drug regulation is important normatively.

Theoretically, this thesis contributes to the studies of pharmaceutical regulation. An analysis in this field usually revolves around the emulation/isomorphism of international guidelines to regulate the sector or the purposive activity of interest groups as influencing policy outcome. However, the social processes discussed in this thesis suggest that the World Health Organization best practices can act as a stimuli for countries to rethink their regulatory norms, but it is domestic political institutions and policy legacies that matter the most as far as the timing and direction of the reform are concerned. Also, the case of Brazil illustrates that actors' preferences (firms and patient groups) that capture the pharmaceutical regulatory process can, by contrast, be shaped by these processes themselves. When facing periods of major economic and political crisis, these groups rethink their demands and their strategies in order to pursue them. As they adapt and learn how to act in the new regulatory environment, they also push the policy path forward.

Lastly, my personal motivation for this research developed after working on a variety of studies related to the politics of HIV/AIDS in Brazil and also a study about lobbying activity in European Union health policymaking (Nunn et al. 2007; Greer et al. 2008). The study of Brazil's AIDS policy contributed to my willingness to

explore how and why this country enacted such controversial regulations as the generic drug policy, whilst the study of lobbying activity provided me with the theoretical and methodological motivation to explore this social phenomenon.

This doctoral thesis might interest political scientists, health policy scholars and economists concerned with the political conflicts in the pharmaceutical sector, but also firms, NGOs, and other institutions concerned with pharmaceutical governance.

The following section provides background information on the content of generic drug policy and an overview of the health system in Brazil. It is important to introduce the elements of a generic drug policy (e.g. policy instruments) and to introduce some contestations around these elements; but most importantly, to situate the case of Brazil within the context of Latin American regulation on this sector. The information regarding the health system in Brazil is important in order to contextualise the institutional background in which this policy was introduced. This will be revisited in detail within the thesis but, for now, it will give the reader a brief overview and guide to further discussions. The final section provides an outline of this research.

## **Background**

### **What is a generic drug policy?**

According to the World Health Organization, a generic medicine is a pharmaceutical product that is no longer protected by a patent, is interchangeable with an innovator drug and can be copied by other companies (World Health Organization 2001). WHO suggest that generic drug substitution should be a key component of a national drug policy in order to address what economics define as “market failure” in the pharmaceutical sector (World Health Organization 2001: 33). In perfect market conditions, buyers and sellers should be able to trade and negotiate their business without government interference, leading to an optimal solution (Bennett et al. 1997; Henry and Lexchin 2002). However, in the pharmaceutical sector this equilibrium would be inefficient mainly for two reasons (Bennett et al. 1997). The first reason is



that, in the pharmaceutical sector, the consumer (or patient) is not in a position to choose directly the product that is needed, relying instead on doctors' expertise to prescribe the best type of product (*ibid*). In turn, doctors rely on information provided from pharmaceutical companies, medical journals or knowledge taught to them at medical schools. Economists call this information asymmetry in the transaction, as the party with better information could manipulate the relationship in order to maximise a particular interest. Secondly, the reason for market failures in this sector is due to the lack of competition created by patent protection, brand loyalty or market segmentation (*ibid*); for instance, brand loyalty promoted by marketing strategies that can lead to market monopoly even after a patent expires. Consequently, the use of generic drugs is usually promoted in the public and private sectors to foster market competition while reducing drug costs, and increasing drug availability and patient access (World Health Organization 2001).

There are two elements of generic drug policy that are used to stimulate market competition: the use of a non-proprietary name and bioequivalence tests. Any given drug has three different names: (i) the chemical name, which describes the product's molecular structure to scientists; (ii) the generic name (or International Non-proprietary Name), which is a shorter, simpler version of the chemical name; and (iii) the brand name, which is assigned by the manufacturer and given trademark protection (usually shorter and easier to remember than the generic name) (Hurwitz and Caves 1998). Each INN is a unique name that is globally recognised and is public property. WHO suggest the use of INN to facilitate the identification of pharmaceutical substances or active pharmaceutical ingredients worldwide (World Health Organization 2010b). For example, the simvastatin developed by Merck is marketed as Zocor®, Simlup®, Simcard® or Simvacor®. The use of INN (or generic name) facilitates a clear identification, safe prescription and the dispensing of medicines to patients, and for communication and exchange of information among health professionals and scientists (World Health Organization 2010). It also allows patients and institutional buyers to shop for the lowest price, as there might be different suppliers of the same pharmaceutical product. Some countries have defined the minimum size of characters in which the INN is printed vis-à-vis the trademark

and advertising (e.g. 30-50% of the brand name size; some countries require equal size for both, while others have adopted a radical approach by abolishing trademarks within the public sector) (World Health Organization 2001; World Health Organization 2010).

The next relevant component of a generic drug policy is the interchangeable/bioequivalence requirement. According to WHO, generic drugs must be therapeutically equivalent to their innovator version, i.e. their rates and extent of absorption do not show a significant difference from their original version. Arguably, bioequivalence gives legitimacy to generic drugs as it implies that one commodity can be replaced for another one, thus establishing the parameters for a market transaction that is based on price (Carpenter and Tobbell 2011: 2). The discussion on interchangeable/bioequivalent tests is rather technical and complex. For the purpose of this study, it is important to understand that the bioequivalence test (BE) indicates that generic drugs will have the equivalent clinical effect with no difference in their potential for adverse effects. Bioavailability tests (BA) establish the rate/extent to which the active pharmaceutical ingredient is absorbed from a pharmaceutical dosage and becomes available in general circulation (World Health Organization 2005). While the former is a parameter to establish equality between two products, the latter refers to the medicines' performance in the human body<sup>1</sup>. This regulatory and scientific parameter was first developed in the United States by the Food and Drug Administration and a network of experts engaged in the generic drug sector during the 1980s to facilitate the entry of these products into the market after patent protection expired (Ascione et al. 2001; Welage et al. 2001; Carpenter and Tobbell 2011). Until then, generic drugs had to go through a similar (and lengthy) process of approval as innovator companies that, most of the time, duplicated the clinical trials that had been done previously.

The generic drug policy can be promoted at various stages from the supply chain to the point of purchase (World Health Organization 2001; World Health Organization

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<sup>1</sup> These parameters are not required for intravenous drugs as they are 100% bioavailable – they are directly introduced in general circulation.

2004c). The policy goal is to encourage target actors to supply and demand generic drugs. For example, a government can promote a mass media campaign to stimulate doctors to prescribe generic drugs or patients to request generic drug substitution (when available). From a supply side, a government can stimulate firms by facilitating registration of these drugs with the National Regulatory Agency or even by committing to give preference to generic drugs in the public procurement of medicines.

The concept of market failure helps to identify situations in which government should intervene in the pharmaceutical sector, thus is frequently used by policy makers as a diagnostic approach (cf. Pindyck and Rubinfeld 2009). Used by the World Health Organization as a normative rationale, it guides member countries on how to identify problems in this sector (market failures) and which solutions should be taken to regulate the pharmaceutical sector. These policy investigations are vital but are only one side of the problem. The deliberation and implementation of INN and bioequivalence tests has proved to be a highly contested effort. Past studies have suggested that a pharmaceutical product marketing budget can be two to four times as large as the budget for its research and development (Comanor 1986), thus firms would be less willing to give up this important component of their business. Because of brand loyalty and the credibility attached to the product, some health professionals, consumers and retailers could be sceptical about the quality of drugs commercialised by generic names. A similar situation is regarding the use of bioequivalence tests (Welage et al. 2001). Studies conducted by international agency advisors argue that current bioequivalence requirements are too stringent and unnecessary for a number of medicines (e.g. some antiretroviral drugs such as ritonavir), which could possibly have sweeping effects on access to medicines in developing countries (Gonzalez and Rossi 2004; Hill and Johnson 2004; Osewe et al. 2008). In other words, besides understanding what regulatory arrangements are necessary to improve access to medicines, it also relevant to understand how countries go about implementing them, i.e. how domestic political institutions (such as intellectual property legacy and health surveillance regimes, or the structure of interest group activity) mediate these external guidelines. In other words, this thesis

is concerned with the governmental approach to these guidelines in relation to its local domestic institution; therefore, the political process to regulate generic drug products.

#### Geographic variations in generic drug regulation

Market competition in the pharmaceutical sector differs substantially between developed and developing countries. In Europe and the United States, intellectual property law was consolidated in the 1950s (Homedes and Ugalde 2005a). Consequently, competition in developed countries starts after patent monopoly expires and involves an innovator versus a generic drug. In this scenario, the introduction of bioequivalence parameters represents a reduction in regulatory requirements in order to register a generic drug, thus accelerating the market entry of pharmaceutical products no longer under patent. By contrast, in Latin America and the Caribbean, for example, intellectual property was introduced (or, for some countries, reintroduced) in 1995 with the creation of the World Trade Organization (WTO) and the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) (Gonzalez et al. 2008). Consequently, market competition in these countries began before the adoption of a patent system. For instance, in Brazil, until 1996, any pharmaceutical firm could manufacture innovator medicines without paying royalties to the research-based firm that developed the drug. These medicines that were copied were not classified as generic drugs as there was no such regulation during this period; they were named similar or “multisource” pharmaceutical products in current WHO terms (World Health Organization 2006).

The introduction of mandatory bioequivalence tests in these countries represented an increase in the normative standards to register pharmaceutical products no longer under patent, regulating a market competition that was already in place. There is a wide variation among countries in the decision as to which products should provide bioequivalence tests and how to implement these tests. For instance, Brazil, Mexico, United States and Canada usually adopt bioequivalence requirements for drugs with

a narrow therapeutic range (NRT)<sup>2</sup> and for highly toxic drugs. From a list of 96 drugs, based on the WHO Essential Medicine List that requires bioequivalence tests, in Brazil 87 products are required to provide bioequivalence tests, followed by Mexico with 59 products, Venezuela with 21 and Argentina with only 15 (Pan American Health Organization 2008a).

Two studies carried out by the World Bank and Pan-American Health Organization advisors in 2003 and 2005 pointed out the differences and similarities in generic drug policy in Latin America (Homedes and Ugalde 2005a; Gonzalez et al. 2008). Brazil, Argentina and Mexico use similar definitions for their pharmaceutical products. Generic is an off-patent drug, therapeutically interchangeable with an innovator product and identified by the INN – Brazil also uses the Brazilian Nonproprietary Name (BNN). In these countries, pharmaceutical products can be divided into three types: innovator drug (patent products); generic drugs (therapeutically equivalent with an innovator drug); and similar or multisource drugs (not bioequivalent, as it may have different form, size or shelf-life). Bolivia, Chile, Colombia, Costa Rica, Ecuador, Nicaragua and Peru classify pharmaceutical products into two types: products identified by a brand name (can be patent or off-patent products) and generics (off-patent drugs identified by INN). Table 1 provides a summary of these different types. In short, in Latin American countries there is no consensus about labelling (brand name or INN) and technical requirements (bioequivalence and bioavailability requirements) for registering generic drug products. Nevertheless, these discrepancies can also be observed in developed countries. For instance, in the WHO Essential Medicines list of 96 bioequivalent drugs, Canada has 92 products that are required to provide bioequivalence, while the US has 88 medicines (Pan American Health Organization 2008a). Although the findings of Brazil's case study cannot be generalised, it can provide important insights into why the generic drug regulation took the form it did and how national institutional and political processes influence the design and implementation of these policies.

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<sup>2</sup> Narrow Therapeutic Range (NRT) drugs “have less than a 2-fold difference between the minimum toxic concentration and minimum effective concentration in blood”. Since small differences in the amount of NTR drug administered may result in more serious consequences than with other ‘uncomplicated’ drugs, the required degree of assurance of equality with its original product is greater [(Corre 2010)].

**Table 1. Types of pharmaceutical products in selected Latin American countries**

Country	Type of pharmaceutical product
<b>Argentina</b>	<p><b>Innovative drugs</b></p> <p><b>Similar drugs (or copies).</b> These have the same active ingredient, concentration, pharmaceutical form and dosage and are used for the same indication as the innovative products. They are equivalent to the innovative product but might differ in size, shape, packaging and period of activity. They are pharmaceutically equivalent to the innovative drug. They may use a brand name.</p> <p><b>Generic drugs.</b> These are drugs that have been proven to be bioequivalent to the innovative drug. They are off-patent and tend to be identified by an INN.</p>
<b>Brazil</b>	<p><b>Innovative or reference drugs</b></p> <p><b>Similar drugs.</b> These have the same active ingredient, concentration, dosage and pharmaceutical form as the reference drug. They are used for the same indications. They are equivalent to the reference drug but may have different size, shape, packaging and excipients. Need to be identified with a brand-name.</p> <p><b>Generic drugs.</b> These are interchangeable with the reference drug and have been proven to have the same efficacy, security and quality. They are produced after patent expiration and are identified with an INN or Brazilian non-proprietary name.</p>
<b>Mexico</b>	<p><b>Innovative or reference drugs</b></p> <p><b>Generic interchangeable.</b> These are interchangeable with a reference product as certified by the Health Secretariat. They are off-patent and are identified by an INN.</p> <p><b>Similar drug.</b> These drugs have the same active ingredient as the reference product and may be identified with a brand name or an INN</p>
<b>Bolivia, Chile, Colombia, Costa Rica, Ecuador, Nicaragua, Peru</b>	<p><b>Branded drugs.</b> These are proprietary drugs and similar or copy drugs.</p> <p><b>Generic drugs.</b> These use an INN or other internationally recognised names. They are off-patent.</p>

Source: Homedes and Ugalde (2005a).

Lastly, the market for generic drug products range from freshly off-patent products (e.g. pravastatin, a medicine to lower cholesterol) to a broad range of older medicines (e.g. acetylsalicylic acid). Contestation can be quite prominent in the first case and limit or delay generic drug competition. A recent illustration is the 2008 European Commission's Pharmaceutical Sector Inquiry (DG Competition), which suggested that innovator companies were using different loopholes in regulatory rules to delay entry of generic medicines into the European market (European Commission 2008). For example, by filing a number of patents for the same medicines, this leaves generic drug producers uncertain as to whether and when they can develop their

products without infringing one of the different patents (ibid). Another example is patent extension contestation, when research-based companies demand restoration of the patent life wasted during the regulatory review process for innovative pharmaceutical products, thus delaying the entry of a generic drug product. Finally, there is also the case of incremental innovation, which can be related to a new therapeutic use of a medicine (also called second medical use) or the improvement in a pharmaceutical product that is already patented; both could be (arguably) the object of a new patent (Correa 2004; Kunisawa 2009). Thus, intellectual property regimes are also important when understanding the process of generic drug regulation as they define which medicines can be legally copied and when. Because these are overlapping regulatory agendas, it is important to observe how they interact and are interpreted by the participants in the policy process in order to understand the extent to which IP agendas matter for Generic Drug regulation.

### **Health system and pharmaceutical reforms in Brazil**

Brazil entered the 1990s with an infant democratic government after 20 years of military government. With the restoration of democracy, a new institutional context was designed with the introduction of the 1988 Federal Constitution (Brasil 1988). It established a highly decentralised political system, involving the transfer of services and resources from federal to states and municipal governments (Avelar and Cintra 2004). It also established check and balance mechanisms with independent Executive, Legislative and Judiciary branches. Furthermore, the new Constitution expanded citizenship rights, including free and universal access to health care (section II of the Constitution). Previously, only 20-30% of the population had access to health care through medical groups, cooperatives or occupational health insurance (Falleti 2010: 41).

The health reform was guided in by a health care movement, or sanitary movement (*movimento sanitario*), organised by intellectuals, health professionals, patients and leftist political parties (Escorel 1999). While some scholars suggest that these health activists had been working for decades and had infiltrated the military government to slowly advance the agenda of universal health coverage (Weyland 1995; Falleti 2010), others argue that the critical period of democratic transition made the health

reform possible (Arretche 2004). For the purpose of this study, it is important to understand that the Brazilian Constitution mandates the right to equal access to health services for all citizens through the Unified Health System (*Sistema Unico de Saude* - SUS). However, in practice, health care provision is still fragmented with a private system coexisting alongside the public. It was estimated that, in 2008, nearly 45 million people (~23% of the population) were covered by voluntary private insurance in Brazil (IBGE 2008). In the same year, total government spending on health represented 44% of the total health expenditure, while private expenditure represented 56% (among this 41.2% came from private insurance and 57.1% from out-of-pocket spending<sup>3</sup>) (World Health Organization 2010c).

Also, although one of the SUS commitments is the provision of pharmaceutical care to the population, over 80% of drug expenses are paid for by out-of-pocket spending (Cohen 2000). In Brazil, it is not mandatory for private health plans to cover expenditure on medicines, leaving this to the discretion of each supplier to define their package of service. To date, there are clauses in a few specific plans to cover up to 30% co-payment for selected drugs in associated drug stores. Rough statistics suggest that, in the early 1990s, 50% of the population had no access to medicines (ALANAC 2010). As Brazil is a country marked by deep inequality, this is also reflected in the skewed profile of drug consumption. For instance, in 1998 income group A represented 15% of the population, and its members consumed about 48% of all pharmaceuticals sold in Brazil's marketplace; group B, meanwhile, represented 34% of the population, and its members consumed about 36% of all drugs sold; and income group C, with 51% of the population, consumed a modest 16% of medicines (Abifarma 1998 in Cohen 2000). Additionally, because in Brazil the Constitution mandates that health is a duty of the state, patients who have been prescribed expensive, sometimes experimental, drugs that are not part of the essential drug lists request in the courts the right to have access to these products (Victora et al. 2011). This obliges the Executive government to purchase these drugs immediately (at times

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<sup>3</sup> The Organization for Economic Co-Operation and Development (OECD) defines out-of-pocket expenditure on health as “cost sharing, self-medication and other expenditure paid directly by private households, irrespective of whether the contact with the healthcare system was established on referral or on the patient's own initiative” (<http://stats.oecd.org/glossary/index.htm>).



without price procurement, as these are patent/unique products), which could represent inefficient use of public sources (*ibid*). In sum, this combination of constitutional right to health care with a skewed access to medicines in a democratic context has turned pharmaceuticals into a highly sensitive political issue, as this thesis will demonstrate.

At the pharmaceutical assistance level, the late 1990s represented a great transformation with the introduction for the first time of a National Drug Policy (Ministerio da Saude 1998). There were significant changes in the financing and delivery of basic medications to the population. Since January 1999, states and municipalities have been responsible for the purchasing and distribution of basic medications. Formerly, this was centralised at CEME (Medicines Central/Ministry of Health), and then under the national *Farmacia Basica* (Basic Pharmaceutical) programme<sup>4</sup> (World Bank 2000). Currently, pharmaceutical assistance is divided into three core components: essential medicines, exceptional medicines and strategic medicines (see [www.saude.gov.br/medicamentos](http://www.saude.gov.br/medicamentos)). The essential medicines component is based on an essential medicines list that includes 375 pharmaceutical products and vaccines. Expenditure with essential medicines is a shared responsibility of three levels of government, while drug procurement and delivery is fully decentralised. The other two components are exceptional drugs (chronic illness, high treatment cost, frequently delivered in secondary/tertiary care, e.g. hepatitis, cancer, epilepsy) and strategic drugs (specific chronic or acute illness, part of Ministry of Health programmes and with established protocols, e.g. AIDS, TB, tobacco). In 2004, a new pharmaceutical assistance model was developed (Brasil 2004). In the *Farmacia Popular* programme (Popular Pharmacy Programme), medicines are sold at the cost of production in government-owned pharmacies (suppliers are public pharmaceutical industries) (Brasil 2004). In 2009, the programme was further expanded to a co-payment system, including private drug stores, covering selected medicines in order to treat diabetes and heart conditions

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<sup>4</sup> Federal government continued to finance strategic drugs for diseases such as AIDS, TB, diabetes, and leprosy.

(suppliers for the Popular Pharmacy Programme-Expansion are usually private pharmaceutical firms, local or multinationals) (Brasil 2009).

At a regulatory level, several important reforms were also introduced in the 1990s as, until then, this sector was poorly regulated. In 1996, Brazil introduced the Industrial Property Act (Brasil 1996a); until then, local pharmaceutical firms could legally copy any drug without paying royalties to the innovator company. This decision was taken after five years of intense debates in Congress that gained much media attention (cf. Revista Veja 1991; Folha de Sao Paulo 1995a). In 1999, motivated by several scandals of fake medicines commercialised in Brazil, and the dissatisfaction with the price of medicines, the Minister of Health proposed several regulatory reforms in this sector (cf. O Globo 1998; Revista Veja 1998; Revista Veja 1998a; Jornal do Brasil 1998b). These included the creation of a National Surveillance Agency and amendments in the Industrial Property Act to facilitate the use of intellectual property safeguards in case of a public health emergency (Brasil 1999a; Brasil 1999b). Also, during this period, Brazil also led important reformulations at international level to clarify the use of intellectual property safeguards and norms related to access to essential medicines (Odell and Sell 2003; Sell and Prakash 2004; Nunn et al. 2009a). It was under this critical context that the Minister of Health also proposed the introduction of a generic drug regulation. Brazil's government activism in pharmaceutical regulation became a common object of study for many political and social science scholars (Biehl 2004; Piovesan and Labra 2007; Bastos et al. 2008; Nunn 2008; Shadlen 2009). However, the political process of generic drug regulation has been under-analysed and has not attracted much interest to date. As such, this study intends to improve the understanding of the policy issues and process of this reform. By focusing on the political process and the stakeholders involved, this thesis explores how and why Brazil promoted such large-scale reform that influenced the sector as a whole and successfully introduced generic drugs into the market (evidenced by the steady increase of the number of sales and volume of these products).

## **Thesis outline**

The first chapter of this thesis provides a critical analysis of the literature on generic drug regulation and contextualises the Brazilian case. It explores the advancements in the study of this pharmaceutical regulatory policy and suggests that a key area of investigation is the political process by which this regulation is discussed and developed. It discusses the two prominent accounts required to study pharmaceutical regulation: the diffusion of international regulatory guidelines and interest group activity, their limitations and inadequacy to explain Brazil's case. Chapter 2 presents the theoretical frame applied in this research, based on historical institutional analysis and constructivism. It proposes an investigation of the regulatory process through a longitudinal perspective, seeking to understand how policy legacies shape the preferences and demands of actors and interest groups. Chapter 3 describes the research protocol required to study the generic drug regulatory process in Brazil. It discusses the methodological choice for the case study and the qualitative research; it also translates the rationale and conceptual parameters presented in the theoretical chapter into a research design. This chapter also describes the research methods, data collection and analysis and further research practicalities (ethical concerns, institutional support).

Chapters 3, 4 and 5 form the empirical core of this thesis. They are organised in order to outline the different stages of generic drug policymaking. Chapter 3 traces the critical period of generic drug reform and its institutional antecedents. It assesses the initial attempts to introduce generic drugs in the early 1990s, the enactment of the Intellectual Property Act in 1996 and the emergence of the HIV/AIDS epidemic. These, together with a scandal involving fake medicines in the late 1990s, which occurred during a particular period of the electoral cycle, were prerequisites for the Generic Drug reform championed by the Minister of Health, Jose Serra, between 1999 and 2002. Chapters 4 and 5 assess the policy effects of this regulatory restructuring, comprising the period between 2003 and 2009. Chapter 5 starts by looking at the institutional context in the 2000s, together with three actors in the generic drug regulation: the government, market demanders (health professionals and

consumers) and suppliers of generic drugs. However, this regulation has also generated unexpected effects on other stakeholders in this sector, such as public pharmaceutical factories and patient advocacy groups, which were clustered for heuristic purposes, and are the objects of the analysis of Chapter 6. Finally, the last chapter summarises the empirical findings and their theoretical and global health implications.

## 1. Contextualising generic drug regulation

This chapter aims to provide a critical analysis of the literature on generic drug regulation and contextualise the Brazilian case. This is important in order to explore the advancements in the study of this pharmaceutical regulatory policy, to identify key areas of investigation and in supporting the research design of this thesis.

The literature that informed this chapter was collected from different sources and was hierarchically consulted, i.e. I started with large indexed databases to grey literature. The first step in reviewing what has been published about generic drug regulation was to look at two large indexed databases, the International Bibliography of the Social Sciences (IBSS) and the U.S. National Library of Medicine (PubMed). Articles indexed in the former tend to be related to economics and social science in general, while the latter usually refer to medical sciences and health policy. The time frame established for this literature review was from 1980 to 2009, given that generic drug regulation first began in the United States in mid-1980 and appeared in the World Health Organization documents also by this period. The key words used were “generic drugs”, “generic drug regulation” and “generic drug policy”. Additional words were included to filter the results such as “economic analysis”, “perception” or “acceptance”, and “pharmaceutical regulation”.

A number of articles were found and all those in which the title or abstract did not refer to regulations of generic medicines *strictu sensu* were discarded. The inclusion criterion also referred to articles published in English, Portuguese or Spanish. An important selection criterion also needs to be clarified here. There are several studies from an intellectual property perspective that make reference to generic medicines. Evidently, as mentioned in the introductory chapter of this thesis, there is an overlapping agenda between these two. Scholars studying intellectual property, public health and access to medicines often mention generic drugs in their papers (cf. Sell and Prakash 2004). Therefore, I consulted these papers and decided to exclude them as their main aim was not to assess generic drug regulation. Also problematic is

the fact that some scholars studying IP or even HIV/AIDS policy, misleadingly classifies products that are not generic drug products as if they were so. For example, they mention Brazil's capacity to produce medicines in local pharmaceutical firms and assume that, because these products are not patented, they are generic drugs (cf. Gomez 2009). This is not accurate, as we shall see in this thesis<sup>5</sup>.

This literature review is organised into three parts. The first part refers to economic studies and attitudes toward generic drug substitution studies. The intention here is not to provide an exhaustive review of these areas but rather to identify the contribution of each of them to the analysis of generic drug regulation. The second part of this literature review refers to policy studies on generic drug regulation. Very few studies of the political process to implement generic drug regulation were identified in the literature review. This type of study is particularly important in clarifying how generic drug policy is discussed, approved and implemented. Because of the limited supporting literature, this section expands the scope of the review to explore broad studies on the regulatory process of the pharmaceutical sector. This is important as it provides an insight into how to assess the regulatory process of generic drugs. To do so, I selected studies from policy scholars that have approached pharmaceutical regulation from a health perspective rather than trade (e.g. intellectual property regulation). I opted for this criterion as the venue for discussing generic drugs is the National Regulatory Authorities/Ministries of Health and because the politics of pharmaceutical regulation can differ substantially when its content is framed as a trade affair.

Lastly, the third part of this literature review focuses on contextualising the case of Brazil. As suggested in the previous chapter, Brazil has one of the most stringent regulatory regimes for generic drugs in Latin America and has promoted significant reforms in its pharmaceutical regulation. This section provides background information about this reform by revising previous studies on this topic. Altogether,

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<sup>5</sup> Perhaps this happens because authors might decide to cluster off-patent medicines into one category (generic drugs) to facilitate the analysis. They may even be unaware of the difference between a similar and a generic pharmaceutical product, thus ignoring the contestation in this sector. If so, this study of generic drug regulation can also contribute to clarifying this and explore why this is relevant.

the three sections of this chapter helped in identifying the avenues of investigation and guided the data collection process.

## **Preceding studies on generic drug regulation**

This section discusses the existing studies of generic drug regulation, consolidating the current understanding of this sector from cross-disciplinary fields and their contribution to understanding this pharmaceutical policy.

### **Economic studies**

Economists have examined the effect of regulation and ask whether government intervention is efficient or more efficient than doing nothing (Noll 1989). Economic analyses are usually concerned with the effects of generic drug competition on the market structure, price and volume of sales. For example, in terms of market structure, economists have suggested that medicines with large sales attract more generic entrants and may have shorter market exclusivity periods than less-selling drugs (Bae 1997; Grabowski and Kyle 2007). In addition, drugs that treat chronic symptoms tend to appear on the market more quickly than those medicines primarily used to treat acute illnesses, and this may be related to the greater stability of their demand over time (Bae 1997). In addition, economists suggest that, in terms of competitive advantage, which ultimately leads to a significant increase in the market share, being the first entrant into this sector is extremely important (Hollis 2002). In terms of price and volume of drugs, there is a lack of consensus among economists. The study of Grabowski and Vernon (1992) suggests that generic producers gain a large market share very soon after patent expiration given the price differentials among original and generic drugs, which are on average much lower. If this is the case, we could expect that innovator drug producers would have an incentive to lower their prices after generic drug competition. Whilst some studies also found this assumption plausible by demonstrating a decline in the prices of original products (Caves et al. 1991), others suggest opposing findings, that the price of original drugs

increases after generic entry into the market and the prices of the generic drugs themselves tend to decline (Frank and Salkever 1997).

Comparative studies of generic drug markets provide evidence of the policy mix that could influence the market penetration of these products. The study of Kanavos *et al.* (2008) is a cross-country assessment, using disaggregated data on price, quantity and sales of selected medicines from IMS (Intercontinental Marketing Services) Health. The authors found that the prices of innovator medicines are not affected by generic competition, while countries with no reimbursement mechanisms have shown greater competition than those that use these mechanisms. Market penetration of generic drugs is fostered by lower generic drug prices, pharmacy competition and higher reference prices (or maximum reimbursement rate). Similarly, Garattini and Tediosi (2000), while comparing five European countries, found that countries with more flexible pricing policies had more success. For example, those with free market mechanisms for wholesale and retail enhance their competitive market. The study of Hudson (2000) compared the UK, Germany and Japan and suggested that large markets influence the probability of generic drug entry and have an impact on innovator drugs sales. All of these studies highlight the relevance of local regulatory regimes and pharmaceutical assistance policy in influencing market penetration of generics (cf. Grabowski and Vernon 1992). Examples of these include the incentives to prescribers offered by the British National Health Service, or the early entry legislation (Bolar provision) that allows generic manufacturers to complete regulatory requirements prior to patent expiry in the US and several European countries (Garattini and Tediosi 2000: 160; Kanavos *et al.* 2008: 502).

The economic assessment of generic drug regulation is particularly relevant when trying to understand the magnitude of this sector, the direction in which it is evolving (e.g. identify bottlenecks) and, perhaps, guide firms' marketing strategy and public policies. However, these studies are conducted in a political vacuum; there is no discussion on the institutional and interests involved in regulatory activity. Thus, only in-depth analysis within each country could provide an understanding of how and why the institutional idiosyncrasies matter for the development of generic drug



market in these countries. Explaining the political dynamics and the policymaking process of generic drug regulation is as important as understanding the effects of generic drug competition on the price of medicines.

### **“Perception” literature**

A second strand of literature has been developed by pharmacists and health management scholars, who focus primarily on perception (or attitudes) of prescribers, pharmacists and consumers of generic drugs (Gaither et al. 2001; Mott and Cline 2002; Granlund 2009; Chong et al. 2010). Generic drug substitution requires that doctors, patients and pharmacists are informed and willing to exchange one product for another (King and Kanavos 2002). If they have doubts regarding the standards and quality of generic medicines, they are often in a position to refuse them. There are many factors that could influence this decision. Of particular importance is their beliefs about generic drugs and also how they go about demanding them (Kirking et al. 2001).

There are a number of studies that look at these issues. Their methodology varies from primary data collection (surveys) and public opinion polls to meta-analysis with secondary sources to explore the determinants of generic drug substitution. For example, determinants for consumers might include income, level of education, age, etc; whilst for physicians some studies point to the differences between private and government employees (Gaither et al. 2001; Granlund 2009). It is difficult to classify these studies into a neat pattern. Some point to the fact that there is generally support from pharmacists (Chong et al. 2010), whilst other suggests that consumers are still concerned about the safety of these products (Iosifescu et al. 2008). Indeed, countries vary in the policy instruments they use to regulate generic drugs, whilst some allow pharmacists to substitute a prescription with a generic version (e.g. Brazil and some states in the US) and others do not (e.g. Portugal). The study of Al-Gedadi and Hassali (2008) reviewed the literature on pharmacists’ views on generic medicines and found factors such as the pricing and bioequivalence of medicines were taken into account when deciding for generic drug substitution. They suggest that there is a consensus that generic medicines should have the same quality as their correspondent

innovator products. The authors suggest that pharmacists assess this by looking at the government lists (such as the Orange Book in the United States, which names the interchangeable drugs), but they also take into account the manufacturer's reputation (note: given that generic drugs do not have a commercial name, marketing strategies are usually directed to the producer's status). Many studies consulted suggest that mass media campaigns and awareness campaigns targeted at doctors and pharmacists can improve generic drug substitution (cf. Babar and Ahmed Awaisu 2008).

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Some reflections can be drawn from this first part of the literature review. The first two groups of scholars are mainly concerned with the outcome of this policy. Generic drug policy is usually justified by these scholars as an intervention to overcome a market failure (neoclassical economic school) (cf. Dugger 1979). The State regulates the pharmaceutical sector to diminish the negative effects of this failure and increase the welfare of the population. As seen in the introduction of this thesis, the market would be inefficient as suppliers have some sort of advantage in deciding which product they will manufacture (e.g. quality and volume) and define the price of their products in relation to the demand for these products. From this perspective, the role of institutions is understated, while individual and firms' behaviour is explained by deducing them from basic postulates (e.g. utility and profit functions) and initial conditions (e.g. income distribution and price of good) (*ibid*: 900-1). The aggregated effect of maximiser agents (consumers/firms) and their interactions determine equilibrium output and price. Although this approach is important to gain an understanding of policy outcome (price of products, effects on the demand and market structure), it does not take into account important institutions (such as regulatory regimes or health systems) that mediate an actor's behaviour (firms and consumers). Nevertheless, the majority of studies on generic drug regulation are concerned with its economic outcome, and less is known about its process of deliberation and development. The following section now turns to explore the policy studies on generic drug regulation.

## **Generic drug regulation from a political perspective**

The review of the literature found a small number of studies from a political and historical perspective on generic drug regulation. The study of Ascione *et al.* (2001) presents a historical analysis of the American case based on an extensive secondary data review through indexing services. The authors assess the events that preceded the Hatch-Waxman Act in 1984, suggesting that generic drug regulation resulted from the lobbying of the generic drug industry with the assistance of consumer groups that had pressured Congress to enact a legislation that would simplify and accelerate the generic drug approval process (Ascione *et al.* 2001: 569). These authors suggest that the history of generic drugs in the US results from a conflict between economic actors; that is, innovator firms seeking to protect their market share versus a less unified coalition of consumer groups, health professionals and care organisations and generic manufacturers that seek to reduce health care costs in general, or the rising costs of a particular therapy. Another source of conflict is between professionals, with the pharmacists trying to expand their role in health care and dispensing or substituting pharmaceutical products, and those in the medical profession trying to limit pharmacist interference in their prescription practice. Finally, the authors point to the scientific debate within regulatory communities on the comparative efficacy of all pharmaceutical products. Note that these authors do not have a background in policy studies but in pharmacology. Although they provide a rich analysis of the evolution of generic drug policy in the States, they are less concerned with its underlying social and political process.

Carpenter and Tobbell (2011), who have also analysed the American case, provide an in-depth analysis of the historical construction of the bioequivalence concept. The authors suggest that this is a joint scientific and regulatory concept developed within a network of pharmacologists, regulators, lawyers and American policymakers with a stake in generic drugs. They highlight the role of the state in shaping the scientific process, network of regulators and scientists, emphasising the regulatory concept formation. They point out that, during the 1970s, the FDA progressively became responsible for developing a methodology to assess bioequivalence and facilitate the

entry of off-patent drugs into the market. This placed the Federal government as a guarantor of equivalence standards. A negotiation in Congress, through an agreement between both parties (democrats and republicans) and between innovators and generic manufacturers, led to the Hatch-Waxman Act. The nascent generic industry would benefit from a rationalised regulatory application process and a bonus of one year of exclusivity for the firm that first markets the product, while innovator firms would be granted a longer period of brand exclusivity. Progressively, these innovator firms dropped their claims against generic medicines. In another publication, Carpenter highlights the political relevance of the FDA's reputation, suggesting that its guidelines serve as a model to other countries (Carpenter 2010). This includes the diffusion of bioequivalence concept, which would be adopted by other countries taking the US as a benchmark.

Both of these studies highlight two accounts of the pharmaceutical regulatory process. One refers to the diffusion of international regulatory guidelines and the other to positive theory of regulation.

### **Global health and the diffusion of international guidelines**

There is a group of scholars of pharmaceutical regulation who claim that international regulatory standards formulated by developed countries inspire developing countries to revise their local guidelines. This seems intuitively plausible as organisations, such as the European Medicines Agency, the American Food and Drug Administration, the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), set the rules to enable pharmaceutical firms to access the market of developed countries. In addition, the scientific expertise of these agencies can encourage governments to emulate their guidelines.

The study of Brhlikova *et al.* (2007) suggests that Good Manufacturing Practices (GMP) in Nepal and India could potentially harm local production of affordable pharmaceutical products. According to the WHO, Good Manufacturing Practices are regulatory aspects of the drug production process that assure that medicines are

produced according to the quality standards necessary to their use and according to the marketing authorisation rules (World Health Organization 2010d). The authors suggest that Good Manufacturing Practices, widely supported by developed countries and WHO, might represent a market barrier to entry, sustainability and perhaps market expansion of local pharmaceutical firms in India and Nepal. These norms imply costly adjustments, particularly for Nepali firms that focus mainly on the domestic market.

Dan Carpenter (2010) studied the reputation of the FDA for its scientific expertise and responsibility for shaping concepts such as Good Manufacturing Practices and bioequivalence, which are widely used in other countries. The author argues that the organisational image of the FDA – understood as a set of symbolic beliefs about the FDA, embedded in multiple audiences – explains much about its reputation that inspires credibility. Through an extensive historical analysis of the activities of this organisation and how this image was built (e.g. scientific accuracy and stringency that avoided such a drug crisis as the Thalidomide scandal in Europe), he suggests that this has led to countries in Europe and India emulating much of their rules.

Since the late 1980s, WHO has disseminated the idea that the introduction of generic drugs could foster market competition and increase access to essential medicines (cf. World Health Organization 1988). The scientific concept of bioequivalence, developed mainly in the United States, also appears in WHO guidelines. It is not clear how and why this international organisation decided to incorporate them into its best-practices guides. The 2001 document “Guidelines for Developing National Drug Policies” dedicated a section to informing countries of the steps to be taken should they decide to introduce these products (e.g. market supply and demand mechanisms) (World Health Organization 1988; World Health Organization 1998; World Health Organization 2001). The WHO also provides guidelines on the use of non-proprietary names, bioequivalence parameters and further technical specifications of drug registration (e.g. World Health Organization 2005; World Health Organization 2010b). Following the rationale from this group of studies, generic drug policy could

be understood as the emulation by other countries of international organisation guidelines, such as WHO or other respectable agencies from the North.

Diffusion of normative guidelines is not new in the public health sector. For instance, scholars of health reforms credit the World Bank and other international agencies for promoting a neoliberal agenda into the social policy sector in Latin America. This was particularly prominent in the early 1990s, when the Bank attached to the loan agreements policy conditions demanding a reduction in social service spending (health, education and welfare) as these represented a large part of public spending (Buse 1993; World Bank 1993). In brief, the idea that underpinned these policy prescriptions was that the private sector would be more efficient in the provision and development of services than the public sector and that emphasis should be placed into prevention initiatives in spite of expensive curative interventions (World Bank 1993). In this sense, government function in public health would be regulatory, while private corporations would provide medical care services. There are several studies of the effects of this policy transfer (cf. Armada et al. 2001) and whether it has been successful or not (cf. Homedes and Ugalde 2005b).

In sum, two elements in this discussion are important for this thesis. The first refers to a practical aspect of pharmaceutical regulation as a cross border health care business and global health concern. Harmonisation of pharmaceutical regulation is important as medicines (and particularly generic drugs, which are commodity products) are goods that can be manufactured but commercialised in a different country, thus have a direct impact on trading activities of firms and health care more broadly. This is particularly important in the context of economic integration and increased number of bilateral and multilateral trade agreements (cf. Homedes et al. 2005). A common regulatory environment for free circulation of pharmaceutical products might require a harmonisation of its members' rules. In this sense, international agencies such as the Pan American Health Organization have been discussing strategies and norms to conciliate different regulatory norms in Latin American countries (Pan American Health Organization 1997). The guidelines proposed by the World Health Organization and the reputation of the FDA policies in

this segment of the pharmaceutical sector could facilitate this process of harmonisation, as these are legitimate and credible models. However, despite this increasing concern with harmonisation of regulatory rules and available models of regulation, little is agreed between member countries on how to formulate these norms to secure public health interests (Pan American Health Organization 2008).

The second element observed in these studies refers to how these guidelines are disseminated across countries. Although the authors discussed in this section are more concerned with the practical implications of diffusion and harmonisation of regulatory rules, the theoretical aspect underpinning their analysis resembles “policy diffusion” arguments. A path-breaking study from this perspective is Peter Haas’ epistemic communities (Haas 1992). In short, Haas argues that these communities are networks of experts whose shared ideas underpin their efforts to influence policy. Because policy-makers face multiple problems with several choices and uncertain outcomes, they would turn to these epistemic communities for solutions and reduce uncertainty. In this sense, WHO’s guidelines on pharmaceutical policy and regulatory norms, such as bioequivalence and National Drug Policy, could represent a major blow to the worldwide expansion of generic drug policies.

Within the typology of policy diffusion proposed by Simmons *et al.* (2006), this would be understood as a learning or emulation process as WHO has no enforcement power to force governments to adopt their best practices. On the other hand, transfer of the FDA guidelines to other countries could happen through learning/emulation or even through coercion mechanisms, such as adding as a condition clause to bilateral or multilateral trade agreement to pressure governments to reform their regulatory norms (cf. Vivas-Eugui 2003; Kampf 2007; Krikorian 2008). Additionally, other scholars have gone a step further and argued that the mechanism of policy transfer is a learning activity, i.e. policy-makers take cognitive shortcuts to decide which policy they will emulate (Weyland 2007). Weyland uses case studies of pension and health reforms in Bolivia, Brazil, Costa Rica, El Salvador, and Peru and suggests that decision-makers in these countries adopted coherent, bold, cognitively available foreign policy models because of selective or accidental attention (Weyland 2007: 6). Instead of systematically culling information (e.g. cost and benefits of a policy) as

suggested by classic rational choice models, they tend to rely on models proposed by international organizations for instance. In this sense, decision makers would purposively turn to generic drug policies as a solution to problems governments face in providing access to affordable medicines and reduce health costs.

The international context and best practices on generic drug policy are indeed relevant and of unquestionable influence when decision makers come across their recommendations. In addition, as mentioned in the introduction, there is a certain level of organisational isomorphism between the international recommendation and a country's regulation. Thus, pharmaceutical sector is a crucial case<sup>6</sup> to assess evidences of policy diffusion. If the emulation of international guidelines affects government decisions, it does so in this sector. However, policy diffusion is not sufficient to initiate a regulatory change in pharmaceutical sector and, in reality, there are profound differences in generic drug regulation among countries (cf. Homedes and Ugalde 2005a). The analytical model proposed in this thesis suggests that it is necessary to understand primarily how domestic pharmaceutical regulatory regimes shape the preferences of actors engaged in the policy process in order to understand the extent in which these best practices/international guidelines matter for policy development. In other words, the institutional arrangement in place mediates the adoption of policies proposed by these international organisations/agencies.

Access to political systems and the ability to make winning coalitions are determined by the domestic structure of the country adopting these ideas (cf. Risse-Kappen 1994). Although these are well-established analytical arguments for studying regulation (cf. Vogel 1986; Baron 1993), apparently those health policy scholars concerned with pharmaceutical regulation have not explored them in depth. Although convergence of regulatory activity would be expected, for instance given the market structure of pharmaceuticals (even small regulatory differences can affect the demand/supply of medicines and limit a sector's growth), there are reasons to believe that there are strong national variations on domestic regulatory designs. Variations

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<sup>6</sup> Crucial case refers to the closest a case study can get to confirm a particular hypothesis. If the case evidences that a hypothesis is not true, it can then be plausibly refuted (Eckstein 1975).



occur according to governments, institutional legacies and bureaucracies (Vogel 1996; Levy and Spiller 1996a). These authors argue that normative aspects of regulatory design are deeply related to politics. “Political action shapes regulatory policy and influences its evolution. It is not only present when policies are formulated and laws enacted but later once the policies are implemented” (Baron 1993: 21). For instance, the study of Levy and Spiller (Levy and Spiller 1996) has demonstrated that there is not an optimal standard model to assure regulatory credibility, which is an important element of regulatory governance (the capacity of governments to assure the integrity of contracts or arbitrary expropriation of rents).

The authors argue that regulatory governance and incentives<sup>7</sup> are choice variables for policymakers but these choices are constrained (*ibid.*). The former is constrained by specific institutional endowment of the nation (e.g. legislative, executive, judiciary, and the country’s administrative capabilities) that determines the form and stringency of the country’s regulatory problems and the options to solve them. The incentives are not implemented in a vacuum and are affected by a nation’s endowments, its distributive politics (the extent to which allocative efficiency can be achieved with regulation) and the nature of its regulatory governance (e.g. level of administrative discretion to assure credibility). In this edited book, the authors tested the framework in different settings to explain how and why reform of telecommunication regulation came about in different countries (Levy and Spiller 1996a). They conclude that regulatory credibility is higher in countries that provide strong restrictions to discretionary action of the legislative and executive. In this sense, complicated pharmaceutical reforms such as generic drug policy require the acquiescence of a constellation of domestic agents and institutions. Although WHO or the FDA can indeed inform policy-makers, by looking at domestic structures we can better understand why and how policies developed the way that they did. International models of regulation are incorporated into the analysis of this thesis as stimuli to which Brazil responded rather than a determinant of the reform outcome.

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<sup>7</sup> The authors define regulatory governance as “mechanisms a society uses to restrain the discretionary scope of regulators and to resolve the conflicts to which these restrains give rise” and incentive structure as “rules governing pricing, subsidise, competition and entry, interconnection, and the like” (Levy and Spiller 1996: 4).

### **Positive theories of regulation**

Positive theories of regulation are concerned with the prediction and explanation of regulatory behaviour, rather than regulation as to maximise efficiency as proposed by economists (Baron 1993: 1; Mello 2000: 16). In short, this group of scholars are concerned with the political causes of regulatory policy (Noll 1989). In its simplest form, this political economy approach to regulation explains “regulation as demanded and supplied as a function of interests of those who incur the distribute consequences of policy alternatives” (Baron 1993: 1). The seminal contribution to this literature was the study of Stigler on regulatory capture that assumes that regulation tends to favour economic actors (Stigler 1971). It states that, because regulation necessarily implies a redistribution of income, some groups would benefit while others would bear its costs. Thus, groups with low organisational costs and higher per capita benefits would tend to be more successful in influencing the regulatory process. By contrast, diffused groups, as consumers, would be less likely to influence the process than small and homogeneous ones. For instance, business groups would lobby for regulations to keep potential new entrants out of the market and enable them to raise the price of their own products.<sup>8</sup>

The core theoretical tenet of a positive approach to regulation is neo-economic institutionalism (Muller 1999). The conceptual models of economists assume a rational, purposive behaviour by all relevant agents (consumers, firms, voters, politicians etc) that uses economic theoretic arguments (but not always mathematical) to make predictions about political behaviour, and when necessary apply methods for testing a hypothesis, as normally used by economists (Noll 1989). Thus, the theoretical scope engages disciplines of political science and law associated with the economic assumptions. For example, this literature examines the rules formulated in the regulatory process to reduce ordinary problems that happen in contracts established between firms, regulators, government, consumers or other groups. These problems include asymmetric information and uncertainty,

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<sup>8</sup> Other scholars have expanded this theory by taking into account the fact that politicians/regulators combine the interests of firms and consumers, while others combine normative elements of efficiency to positive emphasis on distribution of rents (Becker 1983; Peltzman et al. 1989; Mello 2000: 16-18).

transactional costs, problems in providing credible commitment and others (Muller 1999).

Additionally, another branch of this literature is less concerned about whether the aim of regulation is to maximise efficiency or transfer wealth to private agents. Their scholars concentrate on the principal-agent problem faced by politicians in trying to assure reasonable bureaucratic compliance with the aims of legislative mandates and regulatory agencies and regulated firms (Noll 1989; Mello 2000). Because contracts between them are frequently incomplete (they do not cover the range of future possible contingency problems), there will always be a chance for opportunistic exploration in this relation (e.g. moral hazard and adverse selection). For instance, according to these scholars, an ordinary problem of regulatory policy is that regulators do not have complete information on the private costs needed to provide services. Thus, one important element in this game is to design regulatory policies that compel agents to reveal their private costs (Laffont and Tirole 1994 in Mello 2000)

Overall, the literature on the positive theory of regulation is vast and has been the mainstream in studies of politics of regulation<sup>9</sup> (Muller 1999: 4). For the purpose of this thesis, it is important to understand that the core tenet underpinning these studies is that all agents behave strategically in order to maximise their utility (e.g. profit, election). It assumes that the economic world is constantly in equilibrium, that the economic agents are able to identify opportunities to achieve their preferences and would always act in a purposive manner. Although this understanding of interactive activity is rather simplified, it has advanced the discipline substantially in the past decades. Yet studies on the policy process of the pharmaceutical sector and other social regulation has received less attention in this field, perhaps due to the considerable uncertainty about the social phenomenon itself and the consequences of its policy alternatives (Baron 1993). Nevertheless, the existing studies on pharmaceutical regulation agree, to some extent, with this notion of actors' identity.

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<sup>9</sup> Comprehensive reviews of this theoretical approach can be seen in Noll (1989), Pitelis (2010) and Baron (1993).

Abraham has published several studies on the politics of pharmaceutical regulation in Britain, Europe and the US (cf. Abraham 1995; 2002; 2007; 2008). He developed the concept of “corporate bias” to explain the social process of regulatory development. In this sense, corporate bias has the meaning: “pharmaceutical industry was, and is, permitted to have privileged strategic access to, and involvement with, government regulatory policy over and above any other interest group; and more often than other factors, the industry was, and is, decisive in determining regulatory policy outcomes (or lack thereof) (Abraham 2008: 873). His studies emphasise heavily the idea that actors engage in the regulatory process to maximise their utilities (Abraham 2008). Assuming that pharmaceutical industries are interested in profit maximisation and patients have objective interests in “drugs having the maximum benefit-risk ratio possible”, the author suggests that the regulatory process in this sector tends to be biased towards commercial interests (Abraham 2002; 2008: 869). For example, in the 1970s, while the FDA rejected or delayed the approval of many drugs, including beta blockers (to treat coronary illness), the British authority constantly approved them (Abraham and Davis 2006). The authors note that, during this period, British pharmaceutical firms contributed heavily to the national balance of trade, thus the government had prioritised the industry’s commercial goals and productivity over patient safety.

Similarly, Dan Carpenter has also studied the politics of pharmaceutical regulation from a rational perspective, but with less emphasis on the role of the pharmaceutical industry as the main driver of the regulatory process. His studies focus on the American case but adopt a more subtle approach to the “capture concept” proposed by Stigler (Carpenter 2004; 2004a). He problematises the capture argument by asking if, in fact, governments favour larger and older producers at the expense of smaller and newer firms, and why regulation may produce such disparate effects (Carpenter 2004a). He modelled a counterfactual scenario in which capture does not exist and the regulatory agency is neutral in respect to different interests, but still regulators act to guard their own reputation for protecting consumers’ safety. Carpenter finds that larger and older companies have an advantageous position in

this hypothetical scenario. In another article, he advances this analysis (Carpenter 2004). He posits that the FDA is interested in maximising its reputation for protecting consumers' safety and public health (considering not just a selfish motivation but also a possible element of altruism). Looking at the pre-approval process of pharmaceutical regulation, he argues that health advocacy groups, more than pharmaceutical firms, influence drug-reviewing time. He suggests that pharmaceutical firms create/foster patient advocacy lobbying, or collude with these groups in pushing for priority status etc: "politically strategic pharmaceutical firms know that industry lobbying is less successful than patient advocacy, and their regulatory behaviour adapts to this fact" (Carpenter 2004: 56). He provides empirical evidence of patient groups that used the media to demand faster approval for a particular product.

Thus, reforms in pharmaceutical regulation represent a crucial case to study theories of interest groups influence. Pharmaceutical firms are reported as one of the most powerful groups in the world for their wealth and capacity to provide rents for political campaigns (Centre for Public Integrity 2008). They operate under a highly politicised environment and as previously mentioned, regulation affects their business more than any other policy (labor policy, for instance). If firms would be prominent to dominate a sector, it would be reasonable to expect that to happen in pharmaceuticals. Nevertheless, a key problem with the positive theories of regulation is the assumption that regulation emerged in order to serve the interests of particular groups. Attributing the outcome of regulatory policy to rational, purposive actors might be incomplete for several reasons. Analysing the process of institutional design based on numerous empirical examples, Paul Pierson presents several limitations for understanding the origins of institutions (in this case, the regulatory norm) as a rational, functional activity (Pierson 2004: chapter 4). Regulation might have multiple or unexpected effects, thus its existence cannot be explained by observing their creator's preference (usually these innovative changes require a coalition or a group of supporters that propose them for different reasons). Its designers might not act instrumentally, for instance they might reflect cultural specificity (this is discussed in detail in the following chapter). Additionally, actors

might change their preferences over time, as institutions remain stable or politicians may change, or a new generation may inherit norms that reflect a predecessor's preferences rather than their own. In this sense, the author suggests that a more promising avenue of investigation is to take a qualitative, historical approach (Pierson 2004: 130-1). By observing the historical circumstances that make the presence of these favourable (or unfavourable) conditions more or less likely, it is possible to better understand the creation of regulatory norm. Thus, to provide valuable inputs to understand why and how large-scale pharmaceutical regulatory norms are created (beyond the narrow assumption that they serve the interests of particular groups) and how these norms reshape (or not) the regulatory environment.

In this sense, Vogel (1996) also questions the capture model of regulatory policy analysis. Particularly problematic, he argues, is its distorted view of public vs. private interests. Because there is no unique public interest (government officials might disagree on how to define this in ways that cannot be understood in terms of their capture by private interests), it is not possible to explain variation in regulatory policy until we understand how government officials in different countries define public interest. Additionally, the author points out that governments themselves can change the preference of interest groups, manipulate their demands, put one group against the other. The narrow models of interest group preference ignore the role of the state as an autonomous actor/structure in the policy process. For example, he found that interest group alignments were roughly similar across countries, even though policy outcomes were different. Looking at public institutions rather than private interests explained better these variations.

Another limitation of the rational theory is that it assumes the policy process as a game where opportunists' agents try to reap benefits out of incomplete contractual rules (principal-agent problem). However, there are reasons to believe that regulation, particularly in the high technological sector, is a collaborative process (Broscheid and Coen 2003; Woll and Artigas 2007; Woll 2008: 46). The authors point out that the changing nature of trade policy - from tariff and liberalisation of markets to construction and harmonisation of regulatory regimes (e.g. intellectual

property and service trade) - also impacts on the way interest groups and governments interact. According to Woll and Artigas (2007), they interact in the context of uncertainty and governments actively request firm participation and depend quite heavily on the information they provide: “Governments gain information and political support whereas firms gain access to the elaboration of a policy issue” (Woll and Artigas 2005: 126). In this context, interest groups need to persuade governments that they are able to collaborate, but this requires credibility, expertise and cooperation. Certainly, this leads to a question on how we can tell whether states acts autonomously or on behalf of private interests groups. According to Vogel (1996) states are relatively autonomous from society, in other words, the ambivalence within society and divisions between societal groups turns state actors as interpreters and referees in a neutral manner. Decision makers bring to their posts particular ideological bias and institutional capabilities, at the same time trying to progress their agendas and satisfying important groups simultaneously. Thus, according to the author it is in this context (institutional and ideological) that state actors interact, which powerfully shape how they interpret the “public interest” and how they pursue it.

In this sense, studies of other regulatory sectors such as services, telecommunications or financial sectors, can provide important reflections to the study of pharmaceutical regulation. For instance, the study of Woll analyses the unexpected support of firms with former monopolies and large domestic markets to economic liberalisation. She compares the cases of telecommunication and airline services in Europe and the United States. Her study innovates by demonstrating that these firms adjusted their demands for protectionism to fit their government’s agenda on liberalisation of markets. Arguing against assumptions of instrumental rationality, Woll shows that interactions between interest groups and government affect the strategy and goals of lobbying on global trade. Similarly, this thesis challenges narrow assumptions of pharmaceutical regulatory process, such as generic drug regulation, as a function of the lobbying activity of self-interested corporations. Instead, an alternative model, developed in this study, starts by looking at the context in which this regulatory policy is proposed and takes the preferences of interests groups (whether firms,

decision makers or patient advocacy groups) as problematic instead of given. In other words, it supports the argument that actors' preferences are socially constructed within the regulatory process.

This section has reviewed the two main analytical approaches to studying pharmaceutical regulation and highlighted their limitations. Analysing the policy process in this sector. The following chapter proposes an alternative theoretical construct that emphasises the construction of actor's preference, domestic politics and institutional legacy as alternatives to explaining the reform and development of pharmaceutical regulation in Brazil.

### **The Brazilian context**

Brazil's relevance in the study of pharmaceutical regulation is manifold. First, the country has had an unusual, remarkable and widely discussed intervention in this sector. As part of these interventions, in 1999, the Brazilian government created a new independent pharmaceutical regulatory agency, began a vehement price negotiation of AIDS medicines with research-based pharmaceutical industries, shepherded an international movement to clarify the TRIPS agreement and approved the Generic Drug Act in 1999 (cf. Dias and Romano-Lieber 2006; Piovesan and Labra 2007; Nunn 2008). In addition, Brazil is one of the few countries in the world with state-owned pharmaceutical industries competing with local and multinational pharmaceutical firms (cf. Kaplan and Laing 2005). Brazil has a vibrant HIV/AIDS activism that has, since the 1990s, held the government accountable to its Constitutional commitment of providing free and universal access to medicines (Galvao 2000). Lastly, Brazil has one of the most stringent generic drug policies among Latin American countries. This is evidenced by the number of products that must provide bioequivalence, the mandatory use of International Non-Proprietary Name (INN) or the Brazilian Non-Proprietary Name (BNN) and by the fact Brazil is one of the few countries that has a law binding these rules<sup>10</sup> (cf. Homedes et al.

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<sup>10</sup> Apart from Brazil, only Ecuador has one but it is not as stringent as the Brazilian; for example, there is no bioequivalence requirement.



2005). All these elements and remarkable policy achievements offer a complex setting where it is possible to test, compare and posit different explanatory variables. For instance, the multiplicity of actors in the pharmaceutical sector in Brazil (public and private firms, national and multinational, government officials, AIDS advocacy) and the possibility of comparing their preferences in different temporal dimensions enrich the study design.

This section places Brazil's case within the literature discussed so far. Similar to the current state of the international literature on generic drugs, Brazilian scholars have focused extensively on the economic efficiency of this policy enacted in 1999 and the attitudes of health professionals and consumers to it. Several studies analysed the economic outcomes of generic drug competition in Brazil<sup>11</sup>. For example, the study of Vieira and Zucchi (2006) suggests that generic drugs enter the market in Brazil costing 40% less (on average) than its innovator version; in addition, this difference increases over time. Similar findings were reported by other economists (Sutton 2004; Monteiro et al. 2005; Miranda et al. 2009). Other authors have found that generic drug competition is particularly important to lower the price of treatment for chronic illnesses such as diabetes and heart conditions, but also noticed that the best-selling generic drugs in Brazil are those in the antibiotics therapeutic class (Montrucchio et al. 2003; Vieira and Zucchi 2006; Rosenberg et al. 2008; Rosenberg 2009).

In Brazil, because a great deal of drug consumption is out-of-pocket, the perception of consumers in demanding, and health professionals in offering/prescribing these products, is crucial to fostering market penetration of these products. A survey conducted by Bertoldi *et al.* (2005) of a population-based sample of adults from a southern Brazilian city suggests that, although the population was aware of these products, there was still little consumption of generics (and also a relative misunderstanding of different types of pharmaceutical products, whether similar, generic or innovator products). In addition, the study of Rosenberg (2009), who surveyed nearly 550 physicians in the city of Rio de Janeiro in 2008, found that

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<sup>11</sup> Detailed information about this will be provided in Chapter 4 of this thesis.

doctors are suspicious of the quality of generic drugs and also demonstrate concerns about whether the pharmacists/drug store will substitute medicines correctly.

Very few studies have focused on explaining the process of the development of this regulatory policy. A review of the literature found two analyses (master dissertations) from a health policy perspective that focus on the events during the period of reform (1999-2002) (Dias 2003; Franca 2004). Both studies place the ministry of health and presidential candidate, Jose Serra, as the main protagonist of the generic drug reform in Brazil in 1999 and both highlight his interest in capitalising on the political advantages of this initiative.

The study of Franca (2004) is based on an analytical framework developed by Walt and Gilson (1994) to analyse health policies<sup>12</sup>. Her intention was to map the context, actors and process to explain why Brazil has decided to implement generic drugs. Overall, Franca concludes that the introduction of generic drug regulation was centralised at the Ministry of Health, with direct engagement of the Minister Jose Serra, who took muscular decisions, ignoring the different interests of the pharmaceutical sector. She concludes that opposition forces were pharmaceutical firms (the study does not mention whether these were national or multinational) and medical class; whilst firms were interested in maintaining profit, the physicians were interested in reinforcing their alliance with these firms. Particularly problematic with this study is that it tends to gloss over these elements, with poor empirical evidence and, at times, ignoring important contextual aspects (e.g. the author does not include the intellectual property law or the AIDS epidemic in her “context table”).

The study of Dias (2003) is concerned with the normative rules enacted by the recently created National Health Surveillance Agency (ANVISA) to implement the generic drugs and is based on documentary research (archive investigation of two newspapers and official documents) and two in-depth interviews (with the former

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<sup>12</sup> Although Franca (2004) mentioned and used Walt and Gilson (1994) as an analytical framework, their article is concerned with reviewing the literature of policy analysis in the health sector. At the end, the authors propose a model based on actors, context and policy content to better understand health policy.

president of ANVISA and the former president of the Brazilian Generic Drug Manufacturers Association). After the approval of the Generic Drug Act in 1999, the Regulatory Agency was responsible for the further expansion of the technical parameters to register generic drugs in Brazil but also for adopting initiatives to foster market competition (e.g. mass media campaigns). Her study is a comprehensive analysis of the several resolutions enacted by ANVISA vis-à-vis market reactions to obstruct the penetration of generic drugs. She highlights the reservations of drug store representatives and firms about this policy. For example, because there was a delay in the supply of generic medicines, as drug stores were not providing information about these products and pharmaceutical companies were not producing them, ANVISA enacted simultaneous resolutions to foster supply. For example, the mandatory display of a list of interchangeable products in drug stores (so the population could learn about these products and demand a substitution if they so wanted) and a resolution mandating generic drug producers to disclose their records of importation and production of these products (Dias 2003: 90).

Dias' (2003) study also compares the World Health Organization guidelines on National Drug Policy (the generic drug policy component) with the Brazilian norms. She concludes that Brazil has implemented virtually all the recommendations (e.g. drug prescription practices, labelling etc) apart from the reimbursement mechanism<sup>13</sup>. Her analysis concludes that the initial success in sales of generic medicine is less related to the WHO diffusion of generic drug policy than to the media support, governmental activism (within the context of electoral campaign) and the flexibility of ANVISA to adapt to market reactions and induce the supply and demand for these products. Similar to Franca (2004), she also places great weight on the role of the Minister of Health, Jose Serra, as a driver of this reform.

Although these two studies provide information about this reform<sup>14</sup>, less is known about the process that channelled Serra's entrepreneur activity in 1999. To ignore

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<sup>13</sup> Pharmaceutical assistance in Brazil is either subsidised or out-of-pocket. Recently there have been two programmes that introduced co-payment mechanisms.

<sup>14</sup> The study of Dias (2003) to a greater extent than the more empirically limited study of Franca (2004).

this is to partially analyse the means by which this policy was discussed, enacted and implemented. By analysing the details of the crucial period of generic drug implementation, it is likely that the role of human agency (the political entrepreneur) in driving this reform will be highlighted (Pierson 2004: 136-7 and 141). These studies have largely ignored antecedent events that might have been a crucial precondition for generic drug reform. For instance, they have also disregarded the failed attempts to introduce these products in Brazil in the early 1990s and the circumstances by which this happened and how this added to the reform taken in 1999 (Decreto 973/93) (discussed in chapter 4 of this thesis). Thus, their analysis is missing the elements that might have facilitated, obstructed or channelled the Minister of Health's entrepreneurial activity. On the other hand, social scientists have been silent about the subsequent political effects of this reform.

Regarding the organisation of the sector, generic drug regulation prompted a considerable rearrangement in the governance of this sector. The study of Quental *et al.* (2008) highlights the influence of generic drugs in prompting the industrial development of local private pharmaceutical firms. The authors present a range of descriptive data to evidence the increasing participation of national firms in this sector (in sales and value). In this sense, the study of Abreu (2004) on the competitiveness of the Brazilian generic pharmaceutical industry points out the fact that local entrepreneurs have had access to the distribution chain, which has facilitated their penetration in the market but has also highlighted the fact that local producers were pioneers in this sector in Brazil. Table 2 presents the evolution of the ranking of pharmaceutical industries in Brazil according to the proportion of market participation. Thus, economists tell us about the vitality of generic drugs in Brazil and also highlight the expressive participation of local private pharmaceutical firms in this market.

**Table 2. Ranking of pharm industries in Brazil (US\$), 1999 and 2005-2009**

Industry	1999	2005	2006	2007	2008	2009	% participation
EMS*	29	5	3	2	1	1	6,59
Sanofi-Aventis	1	1	1	2	2	2	6,24
Ache*	3	2	2	3	3	3	5,68
Medley*	32	7	6	4	4	4	5,67
Novartis	2	4	4	5	5	5	4,1
Eurofarma*	28	9	8	6	6	6	3,90
Pfizer	7	3	5	6	7	7	3,06
Bayer Schering	23	6	7	7	8	8	2,86
Astra Zeneca	19	22	20	15	12	9	2,37
Boehringer	11	8	9	9	9	10	2,24

Source: (Pro-Genericos 2009 - with IMS Health data)

\* Refers to Brazilian pharmaceutical industries.

This overview of the literature on generic drugs within the Brazilian context suggests further avenues for investigation. Despite the political salience of Brazil's activism in generic drug regulation, studies concerned with how this policy evolved and the cumulative effects on the politics of pharmaceutical governance are absent. The few studies conducted are concerned with the crucial period of policy enactment and suggest that the Minister of Health, Jose Serra, and the activism of the Executive government conditioned the reform. There is hardly any evidence that generic drug regulation in Brazil was a response to major interest group activity or the diffusion of WHO best practices, as suggested in the second part of this literature review. The study of Dias (2003) concludes that generic drug regulation should be a policy of government rather than State, suggesting that this initiative could be destined to fade away over time. The concluding section of this chapter discusses the aims of this study.

### **Lessons from the literature review and study aim**

This literature review aimed to place this thesis within the broader scope of generic drug regulation studies and contextualise the Brazilian case. The key message is that, to date, the investigation of the political and social process underlying the generic drug policy has not engaged many scholars in this field. Furthermore, we can also observe from this cross-disciplinary review the complexity of assessing this sector,

which brings together producers, patients, health professionals and government into the policy process. In this sense, much has been said about the economic outcomes of this policy, or what countries should do to implement generic drugs. There is also some relative evidence on perception of health professionals of this policy in different contexts. However, how countries go about implementing generics, and what the arguments are in favour of or resisting this kind of pharmaceutical sector reform, is less known. Despite its evident political salience, the politics of generic drug regulation goes unnoticed and is unresearched. This chapter has reviewed two predominant explanatory approaches that seem inadequate to explain the origins and development of pharmaceutical regulatory policy.

There is a group of scholars of pharmaceutical regulation who suggest that regulatory policy in this sector originates by emulating WHO best practices or the FDA's estimated norms, or even that regulation originates out of the activity of interest groups. A review of what has been said about the case of generic drug regulation in Brazil does not corroborate these explanations. If pharmaceutical regulation is a matter of policy diffusion, then why did Brazil not implement these changes in the early 1990s? Similarly, if interest groups are a crucial condition to reforms, why do previous studies on the Brazilian case focus on political entrepreneurship of the Minister of Health, rather than firms or patient advocacy? Nevertheless, Brazilian scholars had focused on describing the crucial period of reform, rather than reflecting on the underlying social process that led to the reform. A longitudinal investigation, informed by theoretical approaches on pharmaceutical regulation (suggested in this chapter and the following one) will expand these previous analyses of the reform period. One of the specific aims of this thesis, then, is to review and expand the existing analysis on the leadership of the Minister of Health, Jose Serra, as a core condition to the generic drug reform in Brazil.

The comparative reports discussed in the introduction of this thesis suggest that Brazil became one of the most stringent regimes in Latin America (if not the most), where regulation of these products require not just the mandatory use of an INN and exclusion of trademarks but also mandate bioequivalence tests for a range of

products. Scholars have also demonstrated that economic outcomes in this sector are notable (particularly the difference in price between an off-patent and a patent medicine) despite the concerns about the quality and safety of these products. Additionally, it is also suggested that generic drug competition has had a far-reaching impact on the price of some medicines (particularly those to treat chronic disease) and promoted an unexpected improvement in local pharmaceutical firms' industrial capacity. However, we know less about how this policy evolved and influenced the politics of the pharmaceutical sector and, in this sense, there are different reasons why this should be investigated.

First, although pharmaceutical regulation usually is not an object of political partisanship, the generic drug regulation in Brazil is strongly associated with the Minister of Health's political leadership. However, a new administration came to power in 2003 in Brazil, with the election of President Luis Inacio Lula da Silva, and democratic elections decided on his political party's continuity until 2015. If the political entrepreneur, who has been credited as the main protagonist of the generic drug reform, is no longer in a position to influence decision making in the pharmaceutical sector, how can we explain the development of generic drug regulation? Second, another aspect observed in the literature review of the Brazilian context is the successful position of local pharmaceutical firms in the ranking of the generic drug market (Abreu 2004; Quental et al. 2008). There is hardly any evidence that pharmaceutical firms wanted the government to interfere in their trademarks, or even that these local firms were mandating a reform in the regulatory norms to register off-patent medicines in Brazil. The development of pharmaceutical regulation as generic drug policy is a complicated process that requires the consent and participation of a constellation of actors in the regulatory process. Additionally, regulatory policies can produce losers who might try to reverse the policy for different reasons (cf. Patashki 2003). This thesis, therefore, examines how and why Brazil adopted a generic drug policy, examining the regulatory policy process from its genesis in 1990 to the most recent developments in 2009. This thesis is concerned about the political viability and the social processes of this regulatory policy. It proposes an analytical framework that takes into account policy legacies and

understands the preferences of actors as endogenous to the regulatory process. The following chapters will provide the theoretical and methodological parameters to investigate this public policy from this perspective.



## **2. Theoretical framework: preference formation, policy outcome and the study of generic drug regulatory process**

The previous chapter identified gaps in the literature and suggested avenues for investigation. This chapter provides the theoretical parameters used to analyse the regulatory process of generic drugs in Brazil. This is important to guide data collection and advance the research beyond initial impressions. Different from scholars that invoke the emulation of international regulatory guidelines and interest group activity to explain the pharmaceutical regulatory process, this thesis proposes an analytical frame based on policy legacy and preference construction - based on historical institutional analysis. It proposes an investigation of the regulatory process through a longitudinal perspective and takes into account the influence of the policy process on the behaviour of the stakeholders. This analytical approach is also informed by constructivism and studies of regulatory lobbying activity in Europe. This chapter presents the motivation for this analytical framework, how it interacts with the two other alternative explanations, and the parameters to assess the generic drug regulation in Brazil. The chapter closes by summarizing the main argument of this thesis.

### **Policy shapes politics**

To study the regulatory process of generic drugs in Brazil this thesis draws on a historical institutional approach. These scholars posit that the behaviour of political actors is affected by the institutional context in which they interact (cf. Immergut 1998). In this context institutions are defined as “formal rules, compliance procedures, and standard operating practices that structure the relationship between individuals in various units of the polity and economy” (Hall 1986: 19). They also understand actors’ preferences as endogenous, i.e. the institutional arrangement defines where, when and how interest groups matter for the policy agenda/implementation process. This definition embraces the pharmaceutical regulation studied in this thesis. Parameters that regulate generic medicines in Brazil

are at the same time a formal institution (a Federal Law approved by the Brazilian Congress in 1999); a public policy as this law defines the role of the Ministry of Health in promoting its implementation; but also a regulatory regime as its technical standards are designed, implemented and enforced by the National Regulatory Agency.

The choice for using a historical institutional analysis is twofold: firstly, the WHO has diffused generic drug policy as a best practice intervention in pharmaceutical regulation. It describes in economic terms (market failure motivation) how to diagnose problems of competition in the pharmaceutical sector and what countries should do to solve them. However, less is known about how countries can go about implementing them and the political struggles to implement such norms. This institutional analysis also contributes to understanding the extent to which the diffusion of international guidelines on pharmaceutical regulation matter for the development of generic drug regulation in Brazil, in other words, how domestic political institutions mediate the emulation of these guidelines. This is particularly important in Latin American countries where market competition in the pharmaceutical sector is already in place with the similar drug products. An in-depth assessment of the interest groups participating in the policy process, the evolution of their demands and strategies across time, and how they interpret the generic drug policy can help to clarify policy development. In this sense, historical institutionalism allows for a detailed analysis of the interaction between actors providing a broader and comprehensive understanding of the political process. Additionally, a historical institutionalist approach to preference formation provides an overarching analytical framework to investigate the interactions of government, firms, and patient advocacy groups in the making of pharmaceutical regulation in Brazil. Since it does not limit the analysis into particular groups or deduced interests, it allows me to investigate the possible different groups engaged with the regulatory process and whose participation might have not been predicted previously.

Because the vast literature on historical institutional analysis focuses on macro-level phenomena, that is, mechanisms of institutional creation and development (whether

incremental or punctuated) (cf. Pierson 2004; Streeck and Thelen 2005; Immergut and Anderson 2008), it is important to clarify for the reader that this thesis accounts for a micro-level analysis. It is actor-centred and concerned with the preference of political actors (Hall 2005; Katznelson and Weingast 2005). Naturally, this distinction is for heuristic purposes as in looking at the interactions between actors the analyst must also make reference to the institutional arrangements in place (e.g. stable or in process of change) (Katznelson 2003). How these two levels of analysis interact with each other and how this thesis approaches them are discussed later on in this chapter and subsequently in the methodology chapter.

In addition, it is also important to clarify that I do not intend to make inferences on models of interest representation, to categorize interest representation or investigate the effectiveness of institutional arrangements (cf. Olson 1965; Cardoso 1975; Malloy 1977; Cardoso 1986)<sup>15</sup>. Despite the process of re-democratization and significant institutional changes in Brazil's political system, scholars argue that the country still has a legacy of corporatist structure<sup>16</sup>. Methodologically, analysts can aggregate sectoral corporatism to describe the state model; however, just because Brazil has a legacy of corporatism it is not reasonable to assume that this will be reflected in the organization of pharmaceutical sector. Focusing the analysis on actors' preferences allows me to understand and explain the characteristics of the interest groups in the pharmaceutical sector in Brazil.

Nevertheless, the pharmaceutical sector in Brazil is aligned with theories of the informational model and regulatory lobbying. These look at the transmission of information between groups and decision makers in the policy process (Austen-Smith and Wright 1992; Broscheid and Coen 2003). This model would be suitable for understanding pharmaceutical regulation as it assumes that: (1) government officials need information to make decisions in high technological sectors such as

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<sup>15</sup> For a comprehensive analysis of interest representation in Brazil see Schneider (2004) and Power and Mahrukh (2002)

<sup>16</sup> Corporatism refers to a mechanism of interest intermediation between societal groups and government in the policy making process; states use mechanisms (e.g. subsidy and control) to regulate state-group relations (Schmitter 1974; Collier and Collier 1991). However, assuming that an overall state-level amount of corporatism will be reflected in the ways groups organize in a particular sector might not be plausible.

pharmaceuticals where their expertise is limited. Interest groups provide the knowledge needed to regulate this sector. (2) It is costly for regulators to develop expertise in this sector, thus private actors' information can collaborate with them. (3) By shaping the information provided to policy makers, these private groups might be able to influence the regulatory process without spending resources (e.g. campaign contributions) (Broscheid 2006: 93-4). With respect to the possible false information provided by lobbyists, decision makers can minimize this by either carefully selecting representatives whose information they will rely on or rewarding or punishing faulty information (Broscheid and Coen 2003: 170; Broscheid 2006).

However, the concern with the categories of lobbying systems used by Broscheid and Coen (2003) is that they rule out patient groups or other groups that might also participate as information providers. Interest group activity in this sector is broad and intense, involving patient groups, health professionals, firms, health insurances (cf. Baron 1993: 51). However, the authors assume that only pharmaceutical firms have the required expertise to inform the regulatory process, while NGOs and other groups usually participate in systems where the lobbying costs are low and the demand for legitimacy is high (too salient or ideologically/emotionally charged affairs (*ibid.*: 179)). This dichotomous understanding of business vs. societal participation might not be reasonable. In the pharmaceutical realm many NGOs have developed expertise in law, trade and pharmacology that might contribute to regulatory decisions to the same extent as pharmaceutical firms. Consider for example, Knowledge Ecology International, an international non-governmental organization that has extensive highly skilled staff providing technical support to governments on different regulatory aspects (cf. Knowledge Ecology International 2010). Several studies in pharmaceutical regulation point to the participation of NGOs in the regulatory process. The study of Dan Carpenter, as mentioned in the previous chapter, has highlighted the role of AIDS patient groups in in mid-1980's in demanding fast approval process of medicines to treat AIDS (Carpenter 2004). Also Sell and Prakash has highlighted the role of the Access to Medicines coalition (formed by developing countries and NGOs) in demanding clarifications in the use of TRIPS safeguards during the Doha Round in 2001 (Sell and Prakash 2004).

Although these authors use different theoretical lens to analyse the policy process, both acknowledge the role of NGOs as important advocacy group in the pharmaceutical regulatory arena (either intellectual property or health surveillance regulation).

Finally, several studies on AIDS policy in Brazil have pointed to the role of patient advocacy in participating in the policy process (at the same time designing the policy recommendations and demanding access to medicines to treat the disease) (Galvao 2000; Nunn 2008). However, little is known about the role of this vibrant group in the formulation and development of pharmaceutical regulation in Brazil, particularly regarding generic drug regulation, which can have far-reaching consequences to the availability of antiretroviral drugs. Furthermore, Brazil has also a historical tradition of public production of medicines, which represent an additional actor in the policy process (Kaplan and Laing 2005; Flynn 2008). For this reason, I insist that only with an in-depth assessment of actors' interactions in this sector is it possible to understand better the structure of interest representation.

In sum, because this thesis acknowledges that generic drug regulation might influence the preferences and goals of interest groups participating in pharmaceutical regulation; historical institutionalism provides a better framework for this political inquiry. The following section expands the ontological discussion on preference formation vis-à-vis intentional action, and is followed by a description of the theoretical parameters used to operationalise the research.

### **Studying rationality: intentional vs. constructed action**

Roughly, there are two ways in which actors' preferences can be understood; one group of scholars deduce from theory or previous studies the interests for the relevant actors (rational choice theory), while another group of scholars understand that preferences result from the historical process, i.e. they are socially constructed (historical institutionalism and sociological institutionalism<sup>17</sup>) (Steinmo et al. 1992;

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<sup>17</sup> There is a slight variation between these two. I aligned both as they focus on comparative historical analysis and also both understand preference as a socially constructed phenomenon.

Thelen 1999). This ontological distinction makes all the difference when assessing the generic drug policy process as the theoretical parameters and methodological choices also differ according to the nature of the causal relation (cf. Hall 2003). Nevertheless, it is important to mention that not all scholars accept this dichotomous approach to rationality, and efforts have been made to clarify the intersections between them (Hall and Taylor 1996; Katznelson 2003; Katznelson and Weingast 2005). This section presents the arguments of how each of these theoretical lenses understands the identity of political actors and the role of institutions as opposing assumptions. Highlighting their differences helps in clarifying which aspects of the regulatory process this thesis is interested in investigating.

This historical institutionalism suggests that the preferences of political actors are endogenous, that is, the institutional arrangement in place can influence the formation of preference by political actors (Thelen and Steinmo 1992; Immergut 1998; Hall 2005). Preference formation is then understood as the “process by which social actors decide what they want and how to pursue” it (Hall 2005: 129). It is necessary to look at the policy path before the political events/decisions taken and its subsequent period to trace the evolution of preferences. For example, this parameter would require looking at the participants of the policy process before a given reform, what their policy demands were and strategies they adopted to pursue them; and compare these with the subsequent period.

This approach contrasts with scholars who suggest that actors’ preferences are exogenous to the policy process. That is, they have a fixed set of preferences, behave entirely instrumentally to maximize the accomplishment of these preferences, and do so in a highly strategic manner that suggests extensive calculation (cf. Shepsle 1989; Hall and Taylor 1996: 944-945). Rationality assumptions or thin rationality requires actors’ preferences to be consistent, i.e. have no contradictions in their beliefs and desires; take calculated decisions based on probabilities; and interact with other actors following the rules of game theory (Elster 1983: 5-9; Tsebelis 1990: 18). The point of departure in this perspective is to define the preferences of political actors, which is based on theoretical assumptions or previous studies in the field. For

example, firms interested in maximizing profit will engage in strategic interactions (e.g. predicting the movement of competitors) to advance their preferences. While the methodological point of departure for historical institutionalism (HI) scholars is the political context where preferences and demands are voiced, rational choice institutionalism (RCI) scholars assume that individuals are self-interested and their analysis begins by defining their preferences and strategic interactions in a given institutional context<sup>18</sup> (Lichbach 1997).

The RCI model acknowledges that actors might have more than one preference, so it is necessary to define the order of preference (ordering principle). In a preference function individuals would favour policies close to their 'ideal point' rather than those further away; this utility maximization is at the heart of RCI (Elster 1989; Weingast 1998). The rank-ordered principle should respect the following: (a) the observer must be able to compare options available, (b) the actors' alternatives can be said to be comparable if, "for any pair of them, the chooser either prefers the first to the second, the second to the first, or is indifferent between them" (Shepsle and Bonchek 1997: 25-26), (c) that transitivity implies that individuals rank these alternatives from the highest to the lowest preference, which must be consistent. A basic example is: "[...] if A is preferred to B, and B is preferred to C, then this consistency rule requires that A be preferred to C" (Elster 1989; Green and Shapiro 1994: 14-15). This parsimonious approach to rationality allows the analyst to assess different models of interaction. The discussion in the previous section about studies of pharmaceutical regulation is aligned with RCI assumptions to some extent. Although not all scholars refer to this theoretical parameter, they understand that firms and patient advocacy, as rational interest groups and the regulatory policy process is a result, to some degree, of their aggregated political activity (cf. Abraham 2008). For the RCI scholars, institutions matter to reduce uncertainty or coordinating

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<sup>18</sup> There is a slight distinction between Rational Choice Theory (RCT) and Institutionalism (RCI). The strict rational-choice model would, for instance between Congressmen, be just a matter of how much money is going to their different appropriations. The RCI would take into account subtle mechanisms of coalition-building with the majority buying into his game, which would still obey a maximizing principle, but which would also take stock of institutional constraints. Briefly, many scholars nowadays combine RCT with institutional analysis, not all rational choice assumptions claim that institutional incentives and constraints are decisive for political action (cf. Weyland 2002).

functions (Weingast 2002)<sup>19</sup>. At the same time the institutions serve as a frame for an individual's interaction, they also constrain (or facilitate) the choices available to individuals (cf. Elster 1983; North 1990; Green and Shapiro 1994; Shepsle and Bonchek 1997)<sup>20</sup>.

Contrastingly, for HI actors' preferences are not driven by strategic interactions; instead they evolve as events unfold (e.g. past decisions) (Hall 2005). Preferences are then dynamic and complex. Actors decide not because they calculate the utility but because they are constrained by the institutional context and thus, what they want is affected by the political structure. In this sense, "actors' preferences are not just an input to the policy process but a product of it" (Crystal 2003: 429). When the Brazilian government decided to raise the regulatory standards for registering a generic drug, it insisted that no products should have a trademark and that even innovator drugs should present a generic name together with their trademark to facilitate substitution. Pharmaceutical firms could voice against, adapt or even exit the market if they did not like these changes. However, during a period of crisis or significant institutional or policy reforms, the outcomes are uncertain, thus making it difficult to predict or make rational calculations about which preference to chase. This not to say that actors are not utility maximizers but their utility is flexible (cf. Lusztig 1998). Historical institutionalists neither deny the possibility of intentional actions nor posit that preferences are created by institutions. Instead, these scholars argue that actors make sense of their interests through a dependence on the political process and regulatory context, i.e. the content of the rationality is socially constructed (cf. Woll 2008).

As this section has demonstrated, the intention is to assess the content of actors' preference, starting with an analysis of the context where the agents interact. Thus,

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<sup>19</sup> A classic example is the prisoner's dilemma: when rules change (institutions), the prisoner's choice (defeat, cooperate, etc) also changes because these rules structure the choices that will maximize the prisoner's self-interest (Tsebelis 1990).

<sup>20</sup> North (1990) chapter three provides an extensive description of the rational behavior in institutional approach; Green and Shapiro (1994) chapter two provides a brief summary of common assumptions of uses of RC and points of disagreement between scholars; Shepsle and Bonchek (1997) part one gives an accessible description of the "rationality machinery"; finally, for the "philosophy" of rational behavior see the discussion of 'thin rationality' in Elster (1983).



because this thesis understands that the content of rationality is socially constructed, it does not start the analysis by classifying agents' preferences. Evidently, this approach requires an in-depth knowledge of the case and some level of inductive reasoning; these methodological choices are discussed in the following chapter.

### Concepts: interests, preferences and strategies

Before proceeding to the theoretical parameters, it is important to define the concept of preference formation further. Countless studies in socio and political science mention interests, preferences, strategies (and at times tactics) to explain the policy process and interactive relations. In line with the argument of historical institutionalism, which states that policy can shape politics, constructivism theory helps in clarifying these terms. In short, socio constructivism studies the ways in which groups and individuals engage in the construction and interpretation of their perceived social reality (cf. Wendt 1992). As a theory of the sociology of knowledge, socio constructivism uses sophisticated analysis to understand an actor's preferences.

By using this theoretical framework, the studies of Woll (2005; 2008) present the translation path of preference formation and helps to identify which stage of strategic behaviour this thesis will focus on. Woll established the building blocks for studying the construction of business preferences. The option for this theoretical parameter is threefold: first, her study consolidates different literatures from political science on actors' behaviour (a field that has deep overlapping concepts and definitions). Second, it is one of the most complete analyses on the construction of preference. Third, it innovates by presenting elements that allow for the study of the construction of preference, starting with interest to preference, then to strategy. She identified different levels of abstraction to study political actors' behaviour (Woll 2005). The first level is interest, which she claims to be the most basic objective an actor can embrace. These can be fixed (from a minimalist perspective we could say this is "survival") but are usually inaccessible to empirical observation.

When thinking about these basic interests, it is useful to distinguish between the supposed universal base of the assumption, which I choose to call "universal" or "objective" interest, and its subjective translation. Subjective values apply the objective value to the individual situations of a given actor. For example, let us assume that the universal value is survival. A

subjective value would then describe the forms of survival for different units of analysis: the survival of a nation-state is equivalent to the maintenance of sovereignty, the survival of a politician means that he has to remain an actor in the public sphere, the survival of a firm means that it has to be profitable (Woll 2005: 8)

She argues that interests then are relatively stable. However, to be able to make strategic decisions, political actors have to make use of beliefs as to how their desired ends can be pursued. Thus, the second level is preference to make strategic decisions; political actors need to have a set of beliefs as to how to obtain the desired outcome. The process of ‘adding value’ or setting a normative frame is understood here as preference. “Policy preferences are what actually distinguishes actors from each other and permits them to form coalitions or oppositions” (Woll 2005: 8). Preferences can be assessed by reviewing business press releases, interviews or even newspaper articles, where actors state what their claims are and justify them.

To illustrate the application of this concept to pharmaceutical regulation we can examine the study of Sell and Prakash (2004) as an example. Rational choice scholars that deduce the preference of political actors (whether these actors are firms, politicians or consumer/patient groups), while some scholars who are concerned with the social movement participation in the international political economy suggest that non-governmental organizations are driven by values rather than material interests (Keck and Sikkink 1998). Sell and Prakash contests this dichotomous perception of actor’s preferences (“ideas” vs “interests”), where principle goals align with norms/ideas and instrumental objectives with interests. These authors demonstrate how American pharmaceutical firms successfully framed the debate on intellectual property rights by arguing the claim that patents would bring scientific/economic development and cure for many diseases. They promoted this agenda that lead to the WTO’s TRIPS agreement in 1994. On the other hand, a network of NGOs and developing countries during the Doha Development Round in 2001 re-framed the intellectual property debate so as to include the implications to public health (*ibid.*) and access to medicines as a human rights issue (Nunn et al. 2009a). Sell and Prakash do not argue that this are identical actors, but that the distinction between normative/instrumental is artificial. For them, firms are a group that seek to generate

rents and in which shareholders are the ultimate petitioners of this residual, while NGOs are not generating these profits and are not accountable to any single constituency. However, “generating residuals is not the only instrumental objective an institution can follow - NGOs routinely pursue instrumental objectives such as increasing wages and benefits for their members, increasing membership, and increasing rents accruing to their members [...]” (Sell and Prakash 2004: 167). Similarly, this thesis does not make distinction between actor’s normative and instrumental beliefs.

This understanding of preferences then has implications to the strategies groups use in the policy process. Strategy (or tactics for some) is also the final step of Woll’s building block of preference. She argues that this is the instrument an actor might chose (or favour) in a particular context. In other words, it is the concrete strategy for demanding a particular goal. This level is then highly dependant on the interaction with the institutional context (its constraints and opportunities). According to the analysis of Sell and Prakash, the strategies of business in the TRIPS crusade was defined as a demand for patent protection, which was successfully achieved during the political opportunity opened during the GATT-Uruguay Round in 1994 or the access to medicines demands in 2001 to clarify TRIPS safeguards.

Lastly, according to Woll, whilst interests are normally static and inaccessible for empirical observation; preference and strategy are dynamic, greatly related to institutional interactions and accessible by using social science research methods (e.g. interviews, documentary research) (Woll 2005: 10; Woll 2005a: 83). This thesis will then focus on preferences and strategies of pharmaceutical firms and other interest groups participating in the generic drug regulatory process, as these are the two stages accessible through empirical investigation and are constitutive elements of political actors’ interests.

## **Understanding preference formation**

Peter Hall (2005) identifies four propositions that should be taken into account when analyzing preference formation and are suitable to explain both individual and collective action. This section discusses these and introduces insights from socio-constructivism and lobbying literature that help in illustrating the concepts. The methodological choices to assess these abstract concepts are discussed in the following chapter.

### **Multiple effects and multiple interests**

The first element discussed by Peter Hall (2005) is that political actors have multiple preferences (even for a single issue), which can result in multiple effects. Thus, it is likely that when forming a preference over action actors might assess the costs and benefits for all of them. The key point here is that the process of supporting a preference is intimately related to the identity of the political actor. “By choosing to weigh one variable more heavily than another, the actor is simultaneously choosing to assert one dimension of her identity more strongly than another” (*ibid.*: 132-3). This is a crucial concept for this inquiry of pharmaceutical regulation.

As mentioned in the introduction of this thesis, the regulatory agenda of intellectual property and generic drug are related in many instances. For example, pharmaceutical firms can have a range of preferences from trade advocacy to health regulation (e.g. demand patent of incremental innovations or expand the list of medicines that might provide bioequivalence tests). Similarly, governmental officials can have conflicting preferences whether to favour industrial policy of the sector (that requires expensive investment in the sector or concession to innovator pharmaceutical firms) or foster public health through cost-containment mechanisms (cf. Vandergrift and Kanavos 1997; Kanavos 1998). By putting more emphasis on one of these dimensions, e.g. the intellectual property agenda, this side of their preference is highlighted more strongly. Thus, because regulatory agendas can be

related in different ways, it is crucial to access the content of the demands of each group participating in the policy process to understand which elements of IP matters for generic drug regulation and how. Note that this is not a rank of preferences or nested games as rational scholars propose<sup>21</sup>, but rather a constitutive element of who the group is and what they want. Multiple-interests are not just about assessing the costs and benefits of each action but how obtainable they are, i.e., the probability that a government official might respond more favourable to one demand than another (Hathaway 1998; Crystal 2003). Domestic political structures filter/block policy preferences but also affect (determine) what groups will chose in the first place.

Peter Hall also calls attention to the relevance of ‘framing’ in the process by which preferences are formed, that is, how to portray an issue in terms that connects it to other beliefs (Hall 2005). A similar concept is found in the studies of Baumgartner and Jones (1993) (policy image) and also in socio-constructivism theories (“ideas”) (McNamara 1998; Crystal 2003; Sell and Prakash 2004; Woll 2008). “By framing issues in terms designed to evoke a specific identity, the particular position appeals to those who value this identity highly” (Hall 2005: 134). As Jon Elster (1983) presented in his discussion of “broad rationality”, actors must pay some lip service to the common good as it is virtually impossible to express selfish arguments in public debates (e.g. advocate for a policy solution simply because it favours an individual or a group as suggested by rational choice scholars). Elster also brings models of psychology into this discussion. He argues that it is unfeasible to express preference for the common good without acquiring them. To be convinced that these arguments are not fake, actors would have to ‘invoke the power of reason’: “by speaking the voice of reason, one also exposes oneself to reason” (Elster 1983: 36).

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<sup>21</sup> Nested games refer to Tsebelis (1990: 6-8) concept – situation where actors, confronted with different options, does not pick the ones that seems to be the best (or even against its own interests). He argues that potential suboptimal choices are related to a misunderstanding of the analyst who fails to take into account games that are played in multiple arenas. By introducing other arenas where this actor is interacting, choice then appears to be optimal. Tsebelis discussion does not take into account the identity of the political actors but rather the context of interaction. In addition, nested games are independent games, while the historical perspective sees these events as sequent and dependent on one another (as domino effect).

The concept of multiple interests and framing are crucial to study groups and government relations in pharmaceutical sector. Assuming that there are multiple groups participating in the policy process immediately leads to the question of which one would be more influential and powerful. The concept of framing and venue shopping is crucial to understanding elements of power in this context. In this sense, I stretch the argument of Woll (2007) about the power and political resources of business lobbyists to other groups in the policy process. She argues that many analysts rule out elements of power because of its vagueness, thus making it difficult to measure. However, Woll suggests that the perceived success of non-governmental actors' lobbying depends on the governments' receptiveness to their demands, which in turn depends on strategic advantages they see for themselves in the negotiation process. In other words, actors that can provide particular resources (e.g. information) to decision makers in a particular venue are likely to have better chances of influencing the regulatory process. Note that the imbalance of resources between wealthy pharmaceutical firms and (at times underfunded) NGOs is not the core limitation, as long as the latter is able to provide the required information. The framing process is then key to gaining access to venues that are sensitive to the framework provided<sup>22</sup> (Baumgartner and Jones 1993) and forming coalitions (Hall 2005; Woll 2005: 8)<sup>23</sup>.

### **Prevalence of uncertainty**

The second element to study preference construction relates to a key characteristic of the political realm – uncertainty. When we say that an actor (individual or group) took a particular set of actions to maximize their interests, even if we know what their interests were, we need to know why they had any reason to believe these actions would serve their interests (Hall 2005: 135). By contrast, the formation of

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<sup>22</sup> Venue shopping refers to different government departments that can be more or less receptive to a particular policy and that is why framing the demand to graft attention is so important (Baumgartner and Jones 1993).

<sup>23</sup> However, the process here is not to look at the causal role of ideas as distinct from interests (e.g. the WHO in diffusing ideas of generic drug policy) but rather in the constitutive role of ideas (McNamara 1998). While the former implies a methodological analysis of the causal arguments/variable testing, the latter requires process tracing. For a review on idea-oriented approach to political economy see Hall (1997). Ideas distinct from interests implies a methodological analysis of the causal arguments/variable testing, while constitutive role of ideas requires process tracing (Hall 2003, Woll 2008).

preferences involves a process where actors form judgements or interpretation about which means (beliefs) are likely to advance their ends (demands). This involves the development of frames and efforts to persuade others of their soundness. Uncertainty, then, can create deep discrepancies from expected behaviour making it impossible to predict a priori of what political actors want, without knowing the content and structure of social relations (Woll 2008). For instance, periods of crisis in the pharmaceutical sector caused by contingent events (e.g. publicized cases of side effects of a medicine) might prompt the necessity for reformulating or even creating new institutional arrangements. For example, the case of thalidomide that caused many children to be born with malformations led several European states to create National Regulatory Authorities, and regulate the pre-approval of medicines (cf. Krapohl 2007). Introducing new elements to the regulatory regime and the magnitude of change creates uncertainty and actors can pursue different and at times conflicting interests, as it is not possible to predict the outcome. This leads to the third element of preference formation, interpretation.

### **Role of interpretation to preference formation**

The third proposition discussed by Peter Hall is related to interpretation. He argues that any scholar with a reasonable understanding of political theory and a review of the literature is able to deduce what a group of actors might want in a given situation. However, as this chapter has argued so far, preferences are not fixed. Thus, they are developed through a process of interpretation of the circumstances. Interpretation means gradually understanding the situation and options available, using information - as it is discovered - to refine and expand existing beliefs and finally apply them to new problems (Hall 2005: 136). Actors then revise their initial beliefs as new information is known. The heart of interpretation is then to decide whether to abandon existing beliefs in the face of new information or to extend these beliefs to cover it. Hall argues that the changes in actors' preferences vary according to "belief's elasticity" (degree to which an actor is willing to adjust) and the persistence that they are supported. In turn, this is associated with the extent to which previous information has confirmed them, the availability of alternative beliefs, how they are

connected to the actor's identity and the scope of challenge that new information brings.

Similarly, Hathaway (1998) argues, in her dynamic preferences and strategies framework, that the decisions to voice or adjust preferences are related to its perceived chance of success. As discussed in the first postulate, perceived chance of success refers to the receptiveness of the government department to actors' demands, past history of success and ability to frame the demand (which she calls the level of distress). By analyzing these elements, actors decide whether to voice their demands or abandon them and adjust to the proposed institutional arrangement. In sum, this preference formation is an interactive process of experience and (re)interpretation. To demonstrate, a hypothetical example: if a government decides to reduce subsidies to a given sector, firms might voice opposition against it, exit or adapt to it. The decision is taken according to the perception of the government reception to these claims, costs to adapt and new business opportunities, and whether other firms have decided to adapt to it.

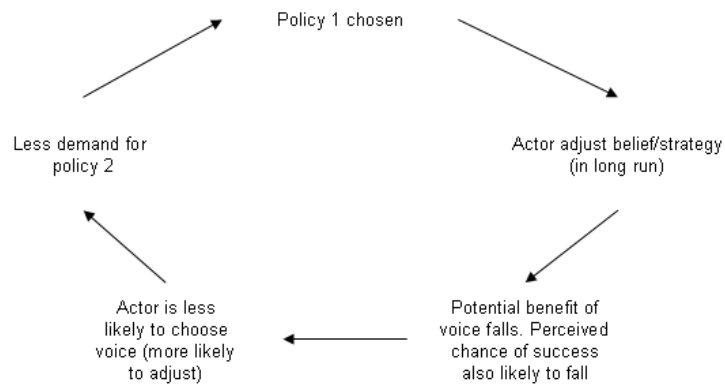
### **Preference formation**

Lastly, the final component is related to the fundamental moment of preference formation. In the political realm, new information comes in the form of an evolving series of events that can confront or corroborate existing beliefs. "New events inspire a double-sided revaluation in which the meanings of those events and of existing beliefs are interpreted in light of each other" (Hall 2005: 136). The problem is to specify what kinds of events are significant in modifying existing beliefs. Hall defines these as 'fundamental eventfulness of preference formation'. How do large-scale reforms contribute to the process of preference formation? The author argues that these events are not meaningful in themselves. Reforms inspire a revaluation of beliefs underpinning existing preferences, thus it depends on how they are interpreted (which, in turn, is conditioned by the context that they occur). If familiar links between beliefs and strategies are broken, it promotes and deepens uncertainty, opening an opportunity for innovative behaviours (Katznelson 2003). In sum, critical events are not the cause of shifts in the preferences of actors by themselves; by



contrast, the way actors interpret these events and the context in which they happen matters. Methodologically, we need to trace the process by which these events shift the perceptions of actors. Figure 1 represents the interaction of the elements presented here.

**Figure 1. Policy effect and preference formation**



Source: Adapted from Hathaway (1998).

These arguments are analogous to constructivism theories, which claim that “the commitment to and the salience of particular identities vary, but each identity is an inherently social definition of the actor grounded in theories in which actors collectively hold about themselves and one another and which constitute the structure of social world” (Wendt 1992: 398)<sup>24</sup>. In this sense, lobbying content and not just lobbying strategies evolve in the course of business-government interaction (Woll 2008).

What all these theoretical discussions tell us is that to analyse the process of generic drug regulation in Brazil, it is necessary to begin by looking at the circumstances by which this policy emerged on the policy agenda. It then proceeds to identify the interest groups participating in the policy process, understanding their multiple demands and strategies (e.g. preferences over INN,

<sup>24</sup> The thin boundary between HI and constructivism is that the latter provides highly sophisticated conceptions of how ideas may matter but constructivists are limited in their empirical scope. On the other hand, HI is concerned with the impact of ideas with more empirical ground but its concepts of idea is, somewhat, limited (Hall 2005: 131).

bioequivalence tests or other alternative solution), how they perceive the Generic Drug Act, and where (which government departments) they voiced these claims. In sum, the political struggle. This provides a base line to compare the content of their demands in the aftermath of reform and seeks groups that support the policy path (how they feedback the generic drug regulation) or those who are dissatisfied with this regulatory arrangement (on what grounds, how and where they complain). Investigating these requires looking at the generic policy process from a longitudinal perspective. The next section discusses the role of temporality in the study of preference formation.

### **The role of temporality in the process of preference formation**

In this section, I advance the relevance of time and context to understand the regulation of generic drugs in Brazil. Katznelson (2003) in the edited volume, *Comparative Historical Analysis in the Social Science*, refers to this analytical step as ‘periodization’. “Microbehaviour, we must continue to remember, requires historical macrofoundation. Yet equally, large-scale comparative analysis is underspecified and incomplete when its microfoundations are left implicit, ad hoc, undertheorized” (*ibid.*: 272). What this suggests is that focusing too narrowly on the interactive process between actors and the policy process as an outcome of this interaction is to present only a partial explanation. Consequently, to clarify the analytical direction of this thesis, the main theoretical theme is the study of the effects of the generic drug regulation and interaction of political actors (firms, patient advocacy groups, government officials or any other actors that participate in the policy process). The background/minor theme relates to the generic drug reform period and development as this is relevant to understanding preference formation. The methodology chapter explains how these two levels of analysis were integrated and investigated in this research. This section deals with the theoretical parameters that bond preferences and policy outcome together.

HI scholars suggest that one would expect policy change to occur only under extraordinary circumstances, when changes in the external environment are so

significant that it overcomes the ‘stickiness’ of existing institutional arrangements<sup>25</sup>.

They refer to these as critical junctures:

[...] *relatively* short periods of time during which there is a *substantially* heightened probability that agents’ choices will affect the outcome of interest. By “*relatively* short periods of time,” we mean that the duration of the juncture must be brief relative to the duration of the path-dependent process it instigates (which leads eventually to the outcome of interest). By “*substantially* heightened probability,” we mean that the probability that agents’ choices will affect the outcome of interest must be high relative to that probability before and after the juncture. [...] (Capoccia and Kelemen 2007: 348 - original emphasis).

In other words, there are short periods in time where institutional constraints are relaxed, deepening uncertainty, and that as a result actors experiment, test, learn and explore different policy alternatives. Once one option is chosen, it is likely to have an extraordinary impact on the subsequent outcomes. In other words, choices made during this critical juncture activate a path-dependent process that constrains future choices. Mahoney (2000) and Pierson (2000; 2004) suggest three elements that constitute a period of critical juncture: (1) contingency, that is, policy change can not be explained by the theory or knowledge that is used. (2) Time and sequence is important as the initial part of a sequence matters much more than final parts - “an event that happens too late may have no effect, although it might have been of great consequence if the timing had been different” (Pierson 2004: 44), while the concept of (3) inertia refers to positive feedback effects – actors adapt to the existing path – that may lead to a single equilibrium; which in turn will be resistant to change.

In this sense, the relevance of this concept to understand actors’ behaviour is that it is in these short periods that political actors can influence policy outcome. For instance, newcomers to the policy process, with distinctive preferences, skills and ideas of alternative paths emerge and redefine the situation. These entrepreneurs can provide policy solutions and create new policies, some of which “endure for extended periods to reshape boundaries, naturalize outcomes, redistribute power and provide new contexts for solving problems [...] not just agency and preferences matter at such times, but particular kinds of innovative competence and patterns of discovery”

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<sup>25</sup> Recent studies on institutional development has moved away from the concept of radical periods of change and path dependence, focusing on the ways in which institutions change rather than remain stable over time (cf. Streeck and Thelen 2005).

(Katznelson 2003: 283). Critical junctures are then windows of opportunity to create policies or change institutionalized policies that for some reason have become undesirable.

However, to be truly considered a critical juncture; political actors must legitimize the new rules. Their feedback stabilizes the policy and institutionalizes the new path (Pierson 2004). As actors adjust to the enacted policy, their identity (preferences and claims) change in ways that reduce the probability that they will demand the antecedent policy in the future. This is the heart of the path dependency concept: once a particular path is chosen, actors adapt to the existing policy in ways that push them further along that trajectory (Thelen 1999). “Public policies generate incentives for interest group activity, influence adaptive expectations and generate distinctive patterns of public support” (Immergut and Anderson 2008: 358). Looking at the aftermath of reform is important because one cannot assume that reforms will be stable. Some critical junctures produce very stable and institutionalized regimes, whilst others seem to contain the seeds of their own destruction (Collier & Collier 1991).

Reforms may be corrupted or reversed after their enactment for different reasons. The organized interests that bear the costs of policy reform do not necessarily vanish after a reform is enacted and they may align themselves with new clienteles who would also benefit if the reform were reversed (Patashnki 2003). In addition, the political entrepreneurs who initially supported the reform may change their minds about the political costs and benefits of serving diffuse interests. Alternatively, they may also find themselves no longer in office (*ibid.*). The “long-term sustainability of any given policy reform rests on the successful reworking of political institutions and on the generation of positive policy-feedback effects, especially the empowerment of social groups with a stake in the reform’s maintenance” (*ibid.*: 203). Sustainability is understood here in the terms of Patashnki (2003) -- the ability of public policy to maintain its stability, coherence and integrity over time, achieving its core goals along with the inevitable vicissitudes of politics.

The concepts of policy change and stability are relevant to this thesis for three reasons. Firstly, dividing the object of analysis into temporal dimensions allows for a comparison of the preferences of pharmaceutical firms and other actors participating in the policy process at different times under the same institutional context. This theoretical-methodological step serves as a frame to understand and compare preferences over generic drugs in different circumstances. Secondly, it helps to explain the generic drug reform, as the literature review has suggested this has been poorly assessed by previous studies and deserves further investigation. Thirdly, and perhaps most importantly, as Katznelson (2003) argued, these are interrelated phenomena, to better understand the policy process, the observer must acknowledge both aspects. Assuming that policy development is a process where actors will feedback the policy chosen, comparing the preferences of different groups participating in the regulatory process after the Generic Drug Act with the antecedent period allows me to assess those who are more active in upholding the path or dissatisfied with it. The literature review provided several reasons to believe that generic drug policy in Brazil could be reversed and why its remarkable economic outcomes are odd. Thus, this comprehensive approach can provide a better assessment of the politics of generic drugs in Brazil.

### **Conclusion – the argument in brief**

The analytical framework proposed in this chapter suggests that it is necessary to understand how regulatory policy legacies shape an actor's preference to be able to understand the extent to which international context and interest groups activities matter for policy development. This longitudinal perspective allows for an assessment of the actors participating in the pharmaceutical regulatory process in Brazil, an understanding of the content of their demands and how they behaved in the pursuit of these claims, and in turn, an assessment of how and why the generic drug reform and development came about. Theoretically, this thesis proposes an analysis of two different but interrelated social occurrences. The first is preference formation and it argues that it is in the interaction with the policy process that actors define what they want and how to portray their demands, in other words, their preferences

are socially constructed (Hall 2005; Woll 2008). The second is policy outcome and it argues that policy decisions taken in critical periods of reform might become path dependent, that is, once a policy path is chosen, actors adapt to the existing policy in ways that push them further along that trajectory (cf. Pierson 2004).

In summary, the historical narrative proposed in this chapter is articulated as follows. Time 1 refers to the period antecedent to the generic drug reform, i.e. a moment when the status quo of pharmaceutical regulation in Brazil became dysfunctional requiring alternative policy solutions. Participants of the policy process (government, firms, patient advocacy coalition or any other relevant actor such as the World Health Organization) demonstrate preference for alternative solutions and these can range from the preservation of the policy path to other radical policy innovations. However, it is uncertain which option will prevail and its outcome. Previous studies on generic drug regulation in Brazil have explored briefly the antecedents to the reform, thus little is known about the antecedent events and policy options reflected in the reform that happened in 1999.

Time 2 refers to the eventful period of generic drug reform between 1999 and 2002. As this chapter has demonstrated, reforms can be triggered by contingent events and be influenced by the sequence of events happening in the antecedent period. In this moment, one policy is favoured against the others – it could be with or without the support of interest groups – and government shows credible commitments to it. Because the outcome of the policy chosen is highly uncertain, actors are not sure whether to adjust or voice against it. As they are less likely to behave strategically, the crisis created an opportunity to reformulate their policy preferences. The two studies of the generic drug reform mentioned in the previous chapter have emphasised the role of the fake birth control pills scandal and the entrepreneurship of the Minister of Health, Jose Serra (invoking his political ambitions), as crucial conditions to the Generic Drug Act. However, this thesis proposes a more nuanced analysis.

Chapter 4 review and expand the existing analysis on the leadership of the Minister of Health, Jose Serra, as core condition to the generic drug reform in Brazil. It explains how did generic drugs became a policy alternative in 1999? According to the theoretical parameters proposed in this chapter, this thesis posits that the political leadership was channelled by past events happening in Time 1 (by creating opportunities to a particular policy be selected) and by the contingent events (such as the medicine crisis suggested by the other authors). Both happening in a particular moment in time can open a window of opportunity to shift the direction of pharmaceutical regulation. Thus, Serra's entrepreneurship in this case would be circumstantial and could be better understood by looking at the historical policy process rather than a narrow function of his political interests. Besides that, government advocacy signalizes credible commitments to a given policy and this happening in a period of crisis can encourage opposing groups to redefine their preferences. Finally, ending the analysis in the process that led to the Generic Drug Act is to give a partial explanation to the regulatory process. Only by looking at the proceeding period is it possible to understand the political effects of this policy on the pharmaceutical sector.

Lastly, Time 3 refers to the generic drug policy development, i.e. the moment when actors abandon the claims for the antecedent policy or alternative solutions and begin to adapt to the proposed reform. By comparing their preferences and demands against the antecedent period, it is possible to observe if there was or was not a change in their content. Chapter 5 and 6 aim to explain how did generic drug policy developed in Brazil. This thesis posits that generic drug policy development could be explained by the reinforcement of these actors, who might have adapted to the new institutional context. Besides, the generic drug policy might have also created unforeseen consequences that should also be the object of investigation to see how the actors negatively affected by this policy react to the institutionalized policy path (claiming another reform or adjustment to it). While the previous periods had been analysed to some extent by other scholars, the institutionalization of generic drug regulation had not received much attention to date.

The following chapter discusses the methodological dilemmas and choices, the process of data collection and analysis of this thesis.



### **3. Methodology**

This chapter describes the research protocol used to study the generic drug regulatory process in Brazil. The first part of this chapter discusses the methodological choice for the case study and the qualitative research design, justifying why these were relevant to this political inquiry. It also translates the rationale and conceptual parameters presented in the previous chapter into a research design. The second part of this chapter describes the research methods and data collection procedures that were used in this research. The following section presents the data analysis rationale and further research practicalities (e.g. ethical concerns, institutional support).

To study the pharmaceutical sector through the lens of preference formation and from a historical perspective, it is necessary to conduct an in-depth assessment of the case and use some level of inductive reasoning. Consequently, the process of designing the research protocol - questions, theories, methods – was not a fixed linear decision but was rather constantly reflected upon and adjusted as new information was collected (cf. Maxwell 2005). These concerns are also the subject of discussion in this chapter. This thesis relies on rich empirical data, including 57 in-depth interviews with government officials, politicians, pharmaceutical firms, NGO activists, as well as hundreds of government documents, market intelligence quantitative data and newspaper articles collected in Brazil between 2007 and 2010.

#### **Research Design**

The previous chapter indicated that this thesis explores the regulatory process of generic drugs by looking into the micro mechanisms within the causal process. It argues that preferences of actors participating in the regulatory process are socially constructed and by adapting their preferences pro-generic drugs, they feedback policy development. By approaching the social phenomena through these complexities, it also affects how the analysis is constructed and verified (Hall 2003).

If so, the problem this thesis seeks to understand can be best addressed using case study, historical narrative and qualitative methodology.

### **Case study and process tracing approach**

A case study approach refers to the inquiry of a class of events happening in a single or small number of settings (Eisenhardt 1989). Within the Lijphart's (1971: 691-693)<sup>26</sup> typology of case studies, this thesis is positioned in between two ideal types: hypothesis generating case studies and theory testing case studies. By looking at the regulatory process of generic drugs in Brazil, this thesis can provide innovative perspectives on pharmaceutical regulation analysis. As seen in the antecedent chapter, scholars interested in pharmaceutical regulation have paid little attention to the relevance of the collaborative aspect of the regulatory policy process, focusing too narrowly on the input of interest groups' activity to the design of regulatory rules. The previous chapters demonstrated that there are few studies in pharmaceutical regulation looking at how governmental decisions in this sector affect its politics, and similarly, despite the political salience of the generic drug regulation, there is hardly any study from a policy perspective. Thus, this study could contribute to the literature on interest group activity in pharmaceutical sector (cf. George and Bennett 2005: 23-24).

Finally, the research of the Brazilian case can also advance the studies of historical institutionalism on preference formation (or theory testing in Lijphart's typology). Regardless of the fact that historical institutional analysis is a well-established theoretical approach in the social sciences, its explanatory scope has evolved over time (cf. Immergut and Anderson 2008). Consider for example recent studies on incremental institutional change and mechanisms of policy feedback (Pierson 2005; Streeck and Thelen 2005; Thelen and Mahoney 2010). In this sense, although a core tenet of historical institutional analysis is the endogeneity of actors preference (Thelen and Steinmo 1992), there are still many obscure aspects over the process of preference formation. Recent studies have considered this an object of analysis (Hall

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<sup>26</sup> Lijphart (1971) identified six ideal types of case studies according to their position in theory development: atheoretical, interpretative case studies, hypothesis-generating, theory confirming, theory-infirming and deviant case studies.

2005; Woll 2008)<sup>27</sup>. Thus, studying the case of generic drug regulation can contribute to this state of the discipline as a plausible probe frame. According to George and Bennett (2005: 75) “plausibility probe are preliminary studies on relatively untested theories and hypotheses to determinate whether more intensive and laborious testing is warranted”. It is important to clarify here that using historical institutional analysis as a theoretical parameter to assess the case of Brazil could be vulnerable to critics on the case selection bias, i.e. the selection of a case based on the dependent variable that is most likely to fit a theoretical approach. However, if the theory is in need of further assessment, picking a case that serves as a heuristic purpose, challenges or advances its constructs justifies the deliberated choice for a particular outcome (cf. George and Bennett 2005: 23). Nevertheless, there are methodological safeguards that can reduce this bias such as process tracing and this is considered in this chapter.

Having considered these methodological dilemmas, I must emphasize that the use of theoretical approaches in this study serves as a guide to data collection and analysis. In this respect, different perspectives were considered, avoiding tautological logic and leaving the case open to other possible assessment. The ultimate weight of this thesis is to explain the regulatory process rather than propose sophisticated abstract propositions; the theoretical implications of this study are more nuanced. The following section expands the advantages and dilemmas of using case study research for this project.

#### The strengths and limits of case study design

There are advantages and drawbacks of case studies as a method for analyzing this social inquiry. Overall, the use and limitations of case study and small-n research in the social science is an enormous debate among methodologists (cf. King et al. 1994; Mahoney 2000; Brady and Collier 2004). Firstly, case study allows a detailed analysis of the historical process of generic drug regulation. This thesis proposes

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<sup>27</sup> Cornelia Woll does not position her work squarely on this perspective but she does mention it extensively as an analogous approach. She has also made important contributions to understanding the building blocks of preference formation within a socio-constructivist perspective, using regulatory lobbying as an empirical frame.

studying the content of interest groups' demands and the policy outcome resulting from the interaction with government, which requires a significant knowledge of the case. Thus, case study allowed me to dissect the generic drug regulation, devote time to understanding the content of actor's preference and how they evolved in the interaction with the regulatory process. Secondly, case studies are well-equipped to understand rare events (cf. Bennett and Elman 2006). It is very unlikely that the conditions that led Brazil to implement generic drugs and its sustainability will be replicated elsewhere. This is partly due to the contingent element of critical junctures but also because the sequence of events that led to the reform and the effects that unfolded afterwards are unique processes. A third advantage of case study is that it allows for the identification of alternative explanations that were not predicted during the early stage of research design. As aforementioned, there are a number of possible variables related to the "state of world history" and that could possibly influence the pharmaceutical regulation. An in-depth assessment of the case can help in clarifying these or abandoning others. Finally, case study and qualitative methodology are particularly useful when assessing interaction effects within one or few cases (cf. Bennett and Elman 2006). Regulation of the pharmaceutical sector is a complex landscape; it involves at the same time industrial, sanitary and access to medicines policies. Besides these different and controversial stakes, the politics of pharmaceutical regulation also engages a range of political actors from business and patient-advocacy groups to government and international agencies. A case study can provide temporal and in-depth information about how pharmaceutical firms and patient advocacy groups interact with the pharmaceutical regulatory process. By doing so, it allows us to trace the evolution of preferences over the indicated period, which is the core aim of this thesis.

However, the case study of pharmaceutical regulation in Brazil does not provide strong inferences about how particular causes can influence the outcome of generic drug regulation in different settings. This limitation in the variance of the dependent variable in different settings makes it difficult to generalize with some degree of confidence the results of this thesis when compared to other countries (cf. Bennett and Elman 2006: 260). On the other hand, methodologists argue that because path

dependence processes are individualized trajectories that suggest complex events and interactions, case studies can be helpful to explain whether and how a particular variable matter to the policy outcome or social phenomena studied (e.g. preference formation in a given context) (cf. George and Bennett 2005: 25; Bennett and Elman 2006: 260).

#### Process tracing approach and qualitative research design

With respect to methodologies of data collection, the use of qualitative methodology seems to provide some relative advantages in addressing the construction of preference and the study of path dependence. An alternative method to study the interaction of generic drug policy and interests groups would be to use a quantitative approach or regression analysis. The objective of regression analysis is to identify a few causal factors that have led to a particular event. The analyst is concerned with estimating the magnitude of the effect of each variable and the degree of confidence by which this effect can be assured (Hall 2008). In the case of pharmaceutical regulation, the observer would model the preferences of each political actor ex-ante or deduce the causal explanation a priori (respecting the conditions to run this statistical method, for example this small set of causal variables should be independent from each other but powerful to explain the outcome across different cases) (cf. Shipan 2004). However, this methodology is inadequate to explore the object of this thesis for three reasons: firstly, it requires a short and limited time horizon; secondly, it is necessary to define in advance political actors' interests; thirdly, regression analysis does not capture the interactive process between actors participating in the regulatory process. These three preconditions contrast starkly with the purpose of this thesis. In turn, qualitative methods and process tracing seem to be the best means to operationalize this case study.

[...] systematic process analysis examines the process unfolding in the cases at hand as well as the outcomes in those cases. The causal theories to be tested are interrogated for the predictions they contain about how events will unfold. The point is to compare these predictions with observations drawn from data about the world. [...] The point is to see if the multiple actions and statements of the actors at each stage of the causal process are consistent with the image of the world [ontology] implied by each theory (Hall 2003: 393-394).

In other words, process tracing refers to the analysis of histories, archival documents, and in-depth interviews with key informants to examine if the causal process outlined by a given theoretical perspective is empirically validated in the sequence and values of the intervening variables in the case studies. The idea is to identify the intervening causal process – the causal chain – between an independent variable and the outcome of the dependent variable (George and Bennett 2005: 6 and 206). Naturally, it would be unfeasible to trace all the conditions of the path but the analyst should focus on those that seem particularly relevant to the phenomena under investigation.

The process tracing research design is similar to what historians use in their narratives to explain all sets of causal events, defining why the outcome occurred in a particular time and place (Hall 2008). However, in process tracing analysis the inquiry is guided by a theoretical construct, identifying the main determinants of a wide class of outcomes and is concerned in exploring the mechanisms by which those determinants influence the outcome (Hall 2003; 2008). It requires a balance between deductive thinking and analytic induction. Thus, the theoretical parameters discussed in the previous chapter guided the data collection, limiting the number of possible and relevant variables that could be related to the generic drug regulation in Brazil. Simultaneously, inductive reasoning allowed me to observe alternative explanations and reformulate the direction of the analysis (examples are provided throughout this chapter). Note that flexibility in data collection is not a license to be unsystematic; rather this flexibility is “a controlled opportunism in which researchers take advantage of the uniqueness of a specific case and the emergence of new themes to improve resultant theory” (Eisenhardt 1989: 539).

#### The challenge of explaining preference formation:

This qualitative study of the content of actors’ preference and demands is grounded on empirical observation. The previous chapter has already pointed out that different from rational choice scholars that deduce (based on previous studies or theories) the goals actors aim to pursue; historical institutionalists/constructivists work with the revealed preferences. Cornelia Woll (2005a: 100-101) calls attention to the problem

of vagueness in assessing the dependent variable from this perspective. For example, how to define which stakes political actors give more weight to in defining their policy preferences? Woll suggests that vague concepts are a problem faced by many social scientists. For example, the definition of democracy is still a subject of debate in the political science field which despite its problematic definition cannot be ignored. This methodological drawback can be minimized by establishing the context in which the concept is to be used. For example, courts (or even the World Trade Organization) can rule in cases where intellectual property rights violate public interest. Public interest is indeed a subjective concept but we can infer a great deal by looking at the time and contexts where it is used. Similarly, the political activities of business or patient advocacy groups can be a response to the policy process in which they are embedded.

Reducing social facts to variables takes away a specific context and therefore increases the vagueness of a concept. For scientific purposes, this reduction is very important, because it is the only way to make an observed phenomenon comparable to others. Dissecting elements, their variation and their relation to specific outcomes not only clarifies an argument, it is the essence of any social science method itself (Woll 2005a: 101).

For the purpose of this study, isolating the preferences of political actors (e.g. pharmaceutical firms, governmental officials or patient groups) into variables would neglect its interactive dimension. There are no reliable ways to identify political actors' basic interests; however, we can infer a lot about what they want and how they portray their claim from qualitative interviews with the representatives of interest groups and documentary research. Also, preferences can be better understood by looking at the historical context in which they interact (among themselves and with government).

A further challenge of studying preference formation is identifying the relevant players. Whose ideas matter? Evidently the policy making process can engage a broad range of players with different stakes. The case of Brazil is particularly complex as it combines public and private firms, patient advocacy (particularly those with chronic diseases that require long term medical care) and government officials across three branches (Congress, Executive and Judiciary) and levels (Federal,

Regional and Local). The intention of this social science inquiry was not to scrutinize every single actor participating in the policy process, but as discussed above process tracing allows the identification of those relevant for the study outcome. In addition, this broad possibility is beneficial to this study as it increases the changes of assessing the preferences of different political actors, increasing the number of observations. Nevertheless, to narrow down the analysis this study initially relied on the literature review and the documents on the governance of generic drugs (mainly publications from the World Health Organization, Pan-American Health Organization and the World Bank) to identify the major players engaged in the pharmaceutical policy making. This initial research protocol identified that while in the reform period the Minister of Health had a crucial role in enacting the reform; whilst local pharmaceutical firms, despite hardly any evidence that they supported this policy, turned out to be the main supporters of generic drugs in the following 10 year-period following the Generic Drug Act. The following sections will expand these concerns and the choices taken for each time period analyzed.

### **Studying the process of generic drug regulation in Brazil**

The study of preference formation starts by looking at the circumstances of political interaction (cf. Hall 2005). To do so, this study looks at the periods before and after the generic drug reform to trace the elements of preference formation. This within-case comparative design allows me to observe the content of the demands of pharmaceutical firms and other actors participating in the regulatory process and how they justify these claims within different periods but under the same institutional context. The generic drug reform represented a moment of intense debate and controversy in Brazil, adding an element of uncertainty into the analysis. This section describes the analytical steps in detail.

#### **(A) Generic drug reform and its antecedent period**

The first analytical step of this study was to explore and review the period of generic drug reform and its antecedents. This is important to assess political actors' interpretation of generic drugs during this period, which provided base-line



information to understand how their preferences evolved afterwards and to assess if there was a relevant change in the content of their demands.

Because previous studies analyzed the pharmaceutical regulatory reforms in Brazil (cf. Dias 2003; Piovesan and Labra 2007; Nunn 2008), this study builds upon these antecedent analyses but focuses on the regulation of generic medicines. It had already been established that the entrepreneurship of Minister of Health Jose Serra played an important role in pushing the generic drug reform. Journalists and scholars of health policy in Brazil usually mention his protagonism in championing the reform (cf. Dias 2003; Franca 2004). However, how can the preference that emerged by 1999, when Congress finally enacted the contested Generic Drug Act, be explained? Backed by the theoretical parameters discussed in the previous chapter, the first analytical exercise was to identify when the generic drug regulation first appeared on the political agenda of Congress, Executive or Judiciary in Brazil. The analysis sought to identify whom were the political actors participating in the policymaking of the pharmaceutical sector (and generic drug regulation in particular); their demands and how they portrayed these claims (framing preferences and defining lobbying strategies). I have also considered the arguments of the diffusion of the WHO guidelines here, as their influence could be more prominent in the antecedent period of the Generic Drug Act<sup>28</sup>.

Note the inductive component of the research design. Because studies in the pharmaceutical sector suggest that patient advocacy groups are relevant actors in the regulatory process (cf. Carpenter 2004) and the study of Ascione, Kirking et al. (2001) highlighted the role of consumer groups in pressuring for the Hatch-Waxman Act in the US; I decided to explore their participation in regulatory process as well. As in Brazil HIV/AIDS activists have a long tradition of pressuring and holding the government accountable for the provision of antiretroviral drugs (cf. Galvao 2000;

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<sup>28</sup> To trace the role of the WHO and policy diffusion, I requested the interviewees to comment on this international agency role, observed if they promoted events and proposals in Brazil (or international meeting that government officials discussed this issue) that could provide evidence of policy diffusion. While the policy diffusion argument was likely to appear in this stage of the research design, the rational choice perspective was assessed throughout the thesis by observing the actors' preference.

Nunn 2008) and diabetes patients are named as one of the main beneficiaries of generic drug competition (cf. Rosenberg 2009), I decided to investigate their role in this stage of the process too.

This process tracing was particularly important in identifying two analytical elements (cf. Capoccia and Kelemen 2007). First, to reconstruct each step of the decision making process. For instance, which decisions were most influential to introduce generic drugs in Brazil, what were the options available/viable to actors who took them but also clarify both their impact and connection to other decision, and how did actors perceive these decisions? The second element of analysis was to look for contingent events, at critical junctures “decisions are taken in a situation of high uncertainty and unpredictability, given the relaxation of the “normal” structural and institutional constraints on action” (Capoccia and Kelemen 2007: 355). In the period of institutional instability, different decisions are possible leading to different outcomes. Thus, a push for counterfactual analysis could help in identifying consequences of other choices. All these elements are discussed in Chapter 4. Table 3 summarizes this research design rationale.

**Table 3. Research design rationale for assessing the reform period**

<b>Antecedent condition</b>	<b>Agenda setting and reform period</b>
<ul style="list-style-type: none"> <li>• Prepare a base line of actors’ preferences and institutional context against which the generic drug reform and its legacy are assessed</li> <li>• Identify the sequence of events that triggered the reform and actors’ perception of them.</li> </ul>	<ul style="list-style-type: none"> <li>• Identify contingency and crisis that emerged out of the antecedent condition and led to the reform</li> <li>• Analysis of the institutional breakdown and opportunity for actors to influence the agenda setting</li> <li>• Explain why the generic drug policy was chosen</li> </ul>

Source: author’s compilation

**(B) The aftermath of the Generic Drug Act**

Once the mechanism that led to generic drug reform and actor’s perception during this period were identified, the second research step was to explore the aftermath landscape. This dimension of the analysis is explored in Chapters 5 and 6. The analytical exercise was to explore the causality that potentially runs in the opposite

direction, and explore how the effects of generic drug regulatory process (independent variable) might have influenced social-political actors and their preferences/strategies (dependent variables) in such a way that makes policy revision difficult. If there is hardly any evidence of muscular interest group activity demanding generic drugs in the previous period, a support favoring generic drug after government intervention would evidence that, to some extent, actors adjusted their preference in the interaction with the policy process.

Here too it is important to start with the policy circumstances to understand the formation of preferences. The process tracing approach was important to identify events/policy debates that could facilitate and obstruct the development of the generic drug regulation. These events included for instance Congressional hearings, seminars, and official meetings to discuss the stakes on generic drug regulation (the use of INN and interchangeable tests). Additionally, the analysis also took into account intellectual property affairs (e.g. debates over patent extension or patentability criteria) as this can also influence the policy path of generic drugs. For each of these events (or issues) the analytical effort was to trace which actors were involved in the debate, what their role was, what they demanded, how they portrayed their demands, and if it differed from their behaviour before the reform. I was also attentive to reactive sequence, that is, attempts to transform or reverse the path of generic drug regulation (cf. Mahoney 2000). Who were the dissatisfied actors, where did they voice their claims, what were their demands, how did they frame their demands?

Note that this was a moment of policy stability. As discussed in the previous chapter, in these periods preferences became stable and it is possible to observe some elements of rational behaviour (cf. Woll 2008). In addition, it is likely that interaction with government in periods of stability is collaborative rather than pressure lobbying or conflict, by engaging in information exchange actors can push forward their claims (Woll 2007) or even build up political advantage (Yoffie and Bergenstein 1985). Thus, tracing the process of generic drug development was also an actor-centred analytical exercise.

The literature review on generic drug policy and the guidelines of the World Health Organization and Pan American Health Organization suggest that the implementation of generic drugs requires the joint support of government (A), consumers (health professionals and patients) (B) and, pharmaceutical firms (C) (World Health Organization 2001; Homedes and Ugalde 2005a). The relevance of each of these players was mentioned in the introductory chapter. As previously justified, I have also included patient advocacy in this stage of the analysis. Thus, these served as a guide to data collection to understand this stage of the regulatory process. Table 4 exemplifies the demands of political actors regarding the generic drug regulation. This list of possibilities is not exhaustive and is merely illustrative.

Note that the best way to assess the support of health professionals and consumers is through public opinion surveys or by designing research projects focusing on their perception (as presented in the literature review). However, this thesis relied on previous studies conducted about this in Brazil, newspaper articles and ad hoc public opinion surveys<sup>29</sup> as a proxy to understand the support or opposition of this group of actors.

**Table 4. Research design rationale for assessing policy development**

<b>Actors</b>	<b>Alternative 1 Support/Adjustment demands</b>	<b>Alternative 2 Dissatisfaction/ Policy revision demands</b>
A. Government (Congress, Judiciary, Executive)	1. Mass public campaigns pro-generics 2. Priority to generic drugs in governmental bids	1. Lack of campaigns to inform people about generic substitution 2. Focus on other policies to increase access to medicines
B. Consumers (patients, doctors, pharmacists)	1. High market demand for generic drugs 2. Physicians give priority to the prescription of generic drugs	1. Little awareness of generic drugs 2. Lack confidence on the safety/quality of generic drugs

<sup>29</sup> Some of these surveys are private and conducted by market intelligence companies such as the Intercontinental Marketing Services (IMS) that collect worldwide information about pharmaceutical retail market. Thus, I had to either rely on executive summary of these reports, newspaper articles that mentioned their results or business associations that disseminate their findings.

C. Pharmaceutical firms (local/multinational, public/private)	1. Develop an extensive portfolio of generic drugs 2. Support of bioequivalence tests	1. Exit the market 2. Repel bioequivalence tests
D. Patient advocacy groups	1. Demand that government should provide generic drugs 2. Campaigns to inform their constituency about generic drugs	1. Repel bioequivalence tests 2. Lack confidence on the safety/quality of generic drugs

Assessing the regulatory process in a longitudinal perspective and observing all these different stakes and actors was an ambitious project. Although this allowed a comprehensive understanding of the generic drug regulation in Brazil, it also required an in-depth and careful observation of the regulatory process. Thus, a considerable volume of data was collected from different sources and insiders of the regulatory process to inform this research design. The following section explores the methods used and how they informed this research.

## Methods

So far I have discussed how case study and process tracing requires an in-depth approach to the field. This study uses three sources to inform the analysis: documentary research, semi-structured interviews and quantitative data. This section discusses how each of these sources was used and its relevance to answer the research questions.

### Documentary research

The use of documentary sources for this study is justified for several reasons. Firstly, it provided important contextual information about pharmaceutical regulation in Brazil before and after the reform. Secondly, it helped in identifying the relevant political actors and their preferences and demands across the 20 year period studied. Political actors frequently document what they are doing, and there are sets of historical documents that provide rich detail that can be extracted to explain causal phenomena. Thirdly, it was particularly important to draw a baseline list of key-informants to be contacted. For instance, several debates and Congressional hearings were organized during the Parliamentary discussions to approve the Generic Drug

Act. Newspaper articles documented the names of participants, their opinions on this matter and how they justified their demands. This information allowed me to track key informants to interview. Fourthly, documentary research was particularly useful to construct evidence of public opinion about generic drugs. This was crucial to understanding policy development given that a great deal of expenditure on medicines in Brazil is out-of-pocket; thus, consumers/doctors perception of generic drugs cannot be ignored. As collecting primary information would be another doctoral project in itself, I used extensive documentary information to assess this aspect of the regulatory process. This study used mainly three sources of documentary evidence:

(A) Newspaper articles. These documents were culled mainly from the Library of Senate and Library of Chamber of Deputies in Brasilia. These libraries provide online and in-site consultations. The Library of Senate also had specific newspaper-clippings with articles about “medicines” published in major newspapers and magazines in Brazil. These news-clippings were available for public consultation and photocopying. I collected newspaper articles published between the period of 1990 and 2009. I have also consulted documents published previously but it was only in 1990 that generic drugs gained media coverage. An additional source of newspaper articles was a direct consultation to the online archives of three popular newspapers in Brazil: *Valor Economico*, which provides similar content to the Wall Street Journal, assessing relevant evolution of market and business in Brazil; *Folha de Sao Paulo* and *O Globo* are popular newspapers that cover national and local (Rio de Janeiro and Sao Paulo) news. Finally, other sources of news information were selected in websites such as *Consulta Remedios* ([www.consultaremedios.com.br](http://www.consultaremedios.com.br)), government, business association and NGOs media clippings, and Magazines (such as *Revista Veja*, *Isto 'E Dinheiro*, *Epoca Negocios*). Although the majority of newspaper articles consulted were those published in Brazil, I have also used LexisNexis to consult information published in popular international news/magazines. This was important to provide evidence of the global state of pharmaceutical regulation and markets, and major international debates on the

WHO/WTO, as these represent a grid in which the regulatory process of generic drugs in Brazil is embedded.

Relevant articles to this study included those directly related to initiatives to implement generic drugs in Brazil, paying particular attention to those who presented interviews with stakeholders and detailed explanation about government decisions. Additionally, articles not directly related to the research topic but that provided further information on the evolution of pharmaceutical regulation in Brazil were also used, such as news related to intellectual property and the creation of the Regulatory Agency (ANVISA). This was important to identify possible intervening variables. Nearly 1,500 articles were selected. This material will be available for consultation via the author's website ([www.elizemassard.com](http://www.elizemassard.com)).

(B) Legislation, policy statements, court decisions. These are official documents that provide evidence of government decisions on pharmaceutical regulation. Virtually all Federal legislation and regulatory decisions (norms) are available for online consultation (including laws that were reformulated)<sup>30</sup>. The Brazilian Congress also provides transcripts of hearings, floor discussions and votes records (when vote is open). For example, it was possible to access the verbatim transcription of the floor discussions on the day that the Generic Drug Act was passed in 1998, including the position of each deputy (the political party's representatives voted in bill, not Congressmen individually) and why they decided to support the legislation.

(C) Business memos and non-governmental organizations' publications. Another relevant source of information was documents produced by political actors. Interest groups often produce a wide range of material (books, booklets, statements, web-documents) to express their demands and why these demands matter. For example, an important piece of evidence about local producers' preferences was the book produced by the Sao Paulo Syndicate of Pharmaceutical Industries to celebrate its

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<sup>30</sup> Federal legislation is available for public consultation via [www.planalto.gov.br/legislacao](http://www.planalto.gov.br/legislacao). These documents date back to the 1890's. In addition, the Congress website provides public consultation to bills and legislations via [www.camara.gov.br](http://www.camara.gov.br) and [www.senado.gov.br](http://www.senado.gov.br). Finally, ANVISA also provides online consultation to decisions taken since Brazil began regulating pharmaceuticals, this are available via [www.anvisa.gov.br/legis/index\\_as.htm](http://www.anvisa.gov.br/legis/index_as.htm).

73rd anniversary (*Sindusfarma: milestones and accomplishments*) (Sindusfarma 2006). This book provided detailed information about regulatory decisions in the pharmaceutical sector, the position of the association, and interviews with key businessmen (board of directors). This publication was important not just to understand their position in particular government decisions but also to identify possible interviewees. Similarly, the Brazilian Interdisciplinary AIDS Association publishes a number of booklets with information about their perspective on intellectual property affairs and pharmaceutical norms. Table 5 provides a picture of the sources consulted.

**Table 5. Summary of documentary research**

Source	City	Documents
Library of Federal Senate	Brasilia	Newspaper, magazine, journals clipping
Library of Federal House of Representatives	Brasilia	Newspaper, magazine, journals clipping
Library of the Ministry of Health	Brasilia	Official documents
Library of the National School of Public Health	Rio de Janeiro	Books, scientific journals and official documents
Scielo	<a href="http://www.scielo.br">www.scielo.br</a>	Scientific journals
Consulta Remedios	<a href="http://www.consultaremedios.com.br">www.consultaremedios.com.br</a>	Newspaper clipping
Confederacao Nacional do Comercio de Bens, Servicos e Turismo (Diario Legislativo)	<a href="http://www.portaldocomercio.org.br/dlg">www.portaldocomercio.org.br/dlg</a>	Clipping of Parliamentary decisions culled by a trade association
Grupemef Magazine	<a href="http://www.grupemef.com.br/">http://www.grupemef.com.br/</a>	Pharmaceutical sector magazine
ComCiencia Magazine	<a href="http://www.comciencia.br">http://www.comciencia.br</a>	Scientific journalism magazine
BNDES clipping	<a href="http://www.bndes.gov.br/SiteBNDES/bndes/bndes_en/Institucional/Press/">www.bndes.gov.br/SiteBNDES/bndes/bndes_en/Institucional/Press/</a>	Newspaper, magazine
Newspapers (Valor Economico, Folha de Sao Paulo, Financial Times, The Economist, Wall Street Journal, New York Times)	<a href="http://www.valoronline.com.br">www.valoronline.com.br</a> <a href="http://www.folha.com.br">www.folha.com.br</a> <a href="http://www.economist.com">www.economist.com</a> <a href="http://www.nyt.com">www.nyt.com</a> <a href="http://www.financialtimes.com">www.financialtimes.com</a> <a href="http://www.wsj.com">www.wsj.com</a>	Newspaper
Government agencies	<a href="http://www.brasil.gov.br">www.brasil.gov.br</a>	Official documents
Pharmaceutical firms and associations	<a href="http://www.ems.com.br">www.ems.com.br</a>	Books, booklets, business statements
Patient advocacy (e.g. ABIA)	<a href="http://www.abiaids.org.br">www.abiaids.org.br</a>	Books, booklets, advocacy statements

Total documents: ~1400

(D) Scientific journals. Scientific journals were an important source of evidence about consumers' perception of generic drugs (health professionals and patients).



Several ad hoc studies were conducted after 2001 to assess this dimension of generic drug policy (cf. Montrucchio et al. 2003; Bertoldi et al. 2005). I have also consulted ad hoc public opinion surveys requested by the National Health Surveillance Agency and a market intelligence study on public opinion towards generic medicines (ANVISA 2001). Additionally, scientific papers also provided quantitative evidence about pharmaceutical products (generic, similar or original products) purchased by the government (cf. Miranda et al. 2009; Pinto et al. 2010). This is important as the Generic Drug Act demands that the public purchase of medicines must give priority to generic drugs, thus this information can provide a proxy of policy development. When possible, this information was compared against different sources to assure the validity of the information provided.

### **Semi-structured interviews**

An important method to inform this social inquiry was the use of elite interviews, that is, key informants that are close to the policymaking process or that have expertise on the topic in question (Dexter 2006 [1970]). The relevance of interviews for this research was twofold: (1) it helped in guiding the data collection process and refining the arguments of the study; (2) getting insider information and the perspective of the representative of an interest group about a particular matter.

Interviews with key informants were particularly helpful in refining the arguments of this research. While the literature review and theoretical concepts provided the initial guidelines and limits of what sort of information to look for, the interviews showed that it would be necessary for some adjustments in the research rationale. I knew in advance that policy development was associated somehow with policy feedback mechanisms and actors adapting to the policy path, but it was not clear how this happened and the extent of these feedback mechanisms to explain generic drug policy development. During the interview process informants highlighted the crucial role of local pharmaceutical firms and how they became national champions in this sector, leading data collection in this direction. Additionally, during interviews it became clear that although intellectual property affairs is apparently another field of investigation, an analysis of generic drug regulation cannot ignore these aspects of

the pharmaceutical sector. How interests groups balance these two dimensions became clear in the course of interviewing and data collection. This leads to the second relevance of interviewing to this research.

Interviews were also valuable in assessing actors' interpretations of particular events in the pharmaceutical sector. For instance, documentary research showed that there was an unsuccessful attempt to introduce generic drugs in the early 1990's and that this was a highly controversial debate at that time. Many participants of that particular event are still active in the pharmaceutical sector nowadays and could provide important information on what the stakes were at that time, what their demands were and how they portrayed these demands. Additionally, interviews helped me understand how they balance their preferences and their multiple demands, for example on topics related to generic drugs, industrial development and intellectual property. For pharmaceutical firms I could learn which government department was more sensitive to their claims, while government officials clarified why the current administration places less emphasis on generic drug policy.

Finally, interviews assisted in constructing the narrative and building up the analysis of this study. All the interviews were transcribed, allowing me to compare and contrast information and reconstruct the story timeline.

#### The interviewing process

An important step of the interviewing process was the selection of key informants. This study used a purposive sampling strategy to select the key-informants. The sample was stated during the process of investigation and by the theoretical rationale discussed in the previous section (cf. Mason 2002). The selection of informants was based on three criteria: (1) they should be in some degree participant to the making of generic drug regulation; (2) their expertise should be connected to pharmaceutical regulation to various extents; (3) they should have the ability to comment (based on their analytical capacity or personal involvement in a particular event) on topics investigated. As stated previously, some informants were identified during the documentary research stage, for example, participants in debates or Congressional

hearings were contacted for interviews. Interviewees were also selected by referral sampling (the ‘snowball’ method); after each interview the interviewee was asked to give suggestions on further relevant interviewees. I knew at the beginning of data collection that there were three major groups to interview: business actors (pharmaceutical firms); governmental actors (executive, legislative and judiciary) and patient advocacy groups (AIDS and diabetes). Table 6 provides a picture of the 57 interviews conducted by group of informants. I interviewed at least one participant of each group, for example, business actors included representatives of multinational firms (with generic drug portfolio or not), local pharmaceutical firms (similar and generic drug producer) and public firms. Interviews were concluded when informants were not adding new information about the topic and conversations ended up being very repetitive.

**Table 6. Groups of informants according to the number of interviewees.**

<b>Groups of informants</b>	<b>Reform period and its antecedents</b>	<b>After the reform</b>	<b>Total</b>
Government	18	9	27
Business association	4	4	8
Local pharma firm	3	3	6
Public pharma industry	2	2	4
Multinational pharma firms	0*	3	3
Patient advocacy	1	7	8
Scholars	0	1	1
Total	28	29	57

\*Executive posts in multinational firms are quite dynamic, thus difficult to locate the participants after this lengthy time. In addition, these are usually senior placements and some of the identified representatives have passed away. Nevertheless, representatives of business association provided valuable information about multinational firms’ perspectives on attempts to regulate the off-patent products.

The majority of the interviews were conducted between March and August 2009. However, previous conversations with representatives of generic drug manufacturers assisted the design of this research project and other additional interviews with NGOs, government officials and business representatives which were conducted after field research period to clarify ambiguous points. The interviewing process required a significant amount of travelling between three cities in Brazil. While the majority of government officials are based in Brasilia, pharmaceutical industries and associations are located in Sao Paulo. Public pharmaceutical industries are spread

around Brazil, so for convenience reasons I interviewed one based in Rio de Janeiro and another in Sao Paulo. Finally, most patient advocacy groups (diabetics and AIDS) were also located in Rio de Janeiro and Sao Paulo.

Gaining access to informants was a heterogeneous process. Business representatives were open to talk about generic drug regulation and pharmaceutical regulation in general as much as representatives of patient advocacy groups. It was particularly difficult to get access to high decision makers in the Ministry of Health as field research for this project was conducted in the beginning of the H1N1 (swine flu) outbreak, which mobilized most health officials in Brazil (and also around the world). When getting references for further interviews I was careful to follow some guidelines suggested by Dexter (2006 [1970]): get introductions from trusted sources; avoid the intermediary to explain the project (this may cause bias and affect the content of the interview) and ask for favors ('doing favors is the life-blood of Congress-constituency relationship' page 39). Besides getting references from previous interviewees I have also participated in events and seminars where high level representatives of government and business associations would speak. For example, in the anniversary event of the 10 years of the Brazilian Generic Manufacturers Association, in May 2009, virtually all pharmaceutical sector representatives participated. Table 7 provides a summary of events that I participated in. These provided me with valuable opportunities to make contacts and arrange new interviews. Furthermore, the research institute where I was hosted during the fieldwork (FIOCRUZ) helped me to negotiate access to Ministry of Health informants. FIOCRUZ is Latin America's major biomedical research institution, with a strong role in the formulation and evaluation of public policies in the broad field of health policy, as well in the development production, and distribution of generic antiretrovirals all over the country. The interviewing protocol can be found in annex 1 and the list of interviewees is in annex 2.

**Table 7. Events attended during field research**

<b>Event</b>	<b>Institution</b>	<b>City</b>	<b>Date</b>
International Seminar Health Policy and Social Protection	National School of Public Health, Ministry of Health	Rio de Janeiro	23.03.09
Seminar Public and Private partnerships in health policy	Center for Health Studies (CEBES)	São Paulo	23.04.09
Valorization of technology	Farmanguinhos, Public Pharmaceutical Industry	Rio de Janeiro	24.04.09
Public consultation 10 years of Generic Medicine Policy and its implementation	House of Representative	Brasilia	28.04.09
Seminar 10 years of generic medicine	Brazilian Association of Generic Drug Manufacturers (Pro-Genericos)	Sao Paulo	25.05.09
Forum Patent and generic medicine	Federal Senate	Brasilia	18.06.09

### **Quantitative data**

This study also used longitudinal quantitative data to understand the development of generic drug policy. I consulted market intelligence data (most of these reports need to be paid for but some provide samples or the executive summary free of charge), particularly information provided by the IMS Health (Espicom Business Intelligence 2007; IMS 2009). A relevant source of information was provided by Pro-Genericos, which monitors the evolution of the generic drug sector since 2001 (Pro-Genericos 2008; Pro-Genericos 2009). Because the use of Pro-Genericos data alone could be biased (e.g. highlight just the successful aspects of the regulation), I have also consulted and compared these with other references. For example, scientific papers (mainly produced by economists); government documents and some newspaper articles also provided information about the evolution of the pharmaceutical sector in general and the generic drug market (cf. Monteiro et al. 2005; Vieira and Zucchi 2006; Nishijima 2008).

I collected longitudinal information about the market share of generic drugs (volume and price); trade balance; evolution of the ranking of pharmaceutical companies in Brazil (volume and value). The National Health Surveillance Agency provides information about the number of generic drugs registered (by company, country,

year), which was also important to assess how this market evolved. This was particularly helpful to understand the evolution of the pharmaceutical sector before and after the generic drug reform. It was also helpful to evidence how local pharmaceutical firms gained significant market share since the introduction of generic drugs.

## **Data Analysis**

Data analysis for this project was conducted jointly to field research and during the writing up period. During field research, each interview was transcribed verbatim immediately after the conversation. I personally transcribed the majority of interviews as this allowed me to reflect about the information given and highlight key themes of each conversation<sup>31</sup>. This was also important to refine the interview guidelines as new information had been culled. Similarly, during documentary research after each day of data collection the information was organized chronologically, I took notes for relevant facts and events that could build up the research questions.

Following Maxwell's (2005) model of data analysis, I initially developed theoretical categories to organize the information. Maxwell suggests three main forms of organizing data collection. While organizational categories require an a priori definition of codes that will be assessed, substantive and theoretical categories are defined once the researcher is familiar with the case studies. However, substantive categories are descriptive codes of the phenomena studied, while theoretical categories places the coded data into an abstract framework (drawn either from prior theory or an inductive developed theory). For example, first I identified broader themes such as "AIDS activism" and "local pharmaceutical firms" as participants of the regulatory process and events such as "Presidential Decree 973/93", "debates for introducing the intellectual property law 1991-1996". Second, I identified the connection between them and key arguments raised. For example, "Presidential

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<sup>31</sup> Given the large amount of interviews, the short period in between them and the other data collection activities that were happening concurrently; I had to hire assistants to help with the transcriptions. Regardless of the time constraints, I personally transcribed nearly 70% of all the interviews.

decree 973/93” (event)→ “local pharmaceutical industry” and “multinational pharmaceutical industry” (preference: opposition to use of INN because doctors should have the right to prescribe by the trademark)→ counter proposal (demand: suggested a basket of medicines). The main purpose of splitting the data by source and structuring the analysis on main theoretical themes was to push the investigation beyond initial impression. By using structured, diverse sources and a comparative scope I sought to increase the accuracy of the analysis, i.e. a close fit between the theoretical construct proposed with the empirical material collected.

Additionally, every two months short memos were produced about the information that had been collected and discussed with my supervisor (by email). This allowed me to investigate different perspectives to the generic drug regulation, abandon the ones that suggested less explanatory evidence and tailor the key elements for this study. A particular example is the case of public opinion support, as more data had been collected it was becoming clear that the population had limited awareness about generic substitution, lack of confidence on the safety/quality of these drugs (including doctors), thus public opinion assumption would explain less the path of generic drug sector. On the other hand, it was clear that there was a major consensus among virtually all interviewees that local pharmaceutical firms played a significant role in the sustainability of the generic drug sector, and thus deserved further investigation.

A second step of data analysis was taken after the majority of data had been collected. Documentary material was separated into: newspaper articles; scientific articles; governmental documents, and interest groups documents. All this material was organized chronologically. All interviews were transcribed and organized according to the position of the informant in the policy process (some had overlapping tasks -- one informant could have been a government official at one point and then a private sector worker at another point). This second step was to reconstruct the narrative properly, writing up a pure historical description of events and focusing on how each participant of the policy process interpreted them - for example - a particular governmental decision. This allowed me to organize all the

data collected, deepen my knowledge of the case and reorganize the themes/categories in order to develop the final analysis.

A schematic organization of data analysis is presented here to illustrate this stage of the methodology but also to justify the structure of the empirical chapters. Overall, chapters are organized to outline the different stages of generic drug policymaking. The analysis of the generic drug reform period led to the emergence of the following pattern of events, which will be discussed in Chapter 4:

**Table 8. Events discussed in Chapter 4**

Antecedents	Reform	
Sequence of events (1990's)	Contingency (1999-2002)	Reform steps (1999-2002)
Initial attempts to introduce generic drugs in Brazil	<ul style="list-style-type: none"> <li>• Fake medicines scandals and price/cost of medicines</li> <li>• Particular point in the electoral cycle (Presidential election)</li> </ul>	Phase 1 – Parliamentary negotiations and the Generic Drug Act
Enactment of the Intellectual Property Law		Phase 2 – Governmental activism
HIV/AIDS epidemic / treatment		

The narrative of chapter 4 traces how the generic drug regulation came about. The qualitative analysis of these events allowed me to explore in-depth the process that led to the reform. It became clear that the main participants of pharmaceutical regulation at this point of time were pharmaceutical firms and to a lesser extent pharmacists association and other less organized interests (e.g. physicians associations). Their preferences, demands and perspectives are carefully analysed in chapter 4. On the other hand, there was hardly any evidence that HIV/AIDS activists or other disease groups engaged in any aspect of health or trade regulation of medicines over this period, their concerns referred largely to pharmaceutical assistance and claims of access to medicines. However, their demands contributed to put regulation of medicines at the top of the agenda of the Minister of Health, as we shall see. The remarkable governmental advocacy between 1999 and 2002 and the reactions to it are also explored in Chapter 4.

Similar to the analysis of the reform and its antecedent period, the subsequent data analysis began by looking at events and circumstances of generic drug policy

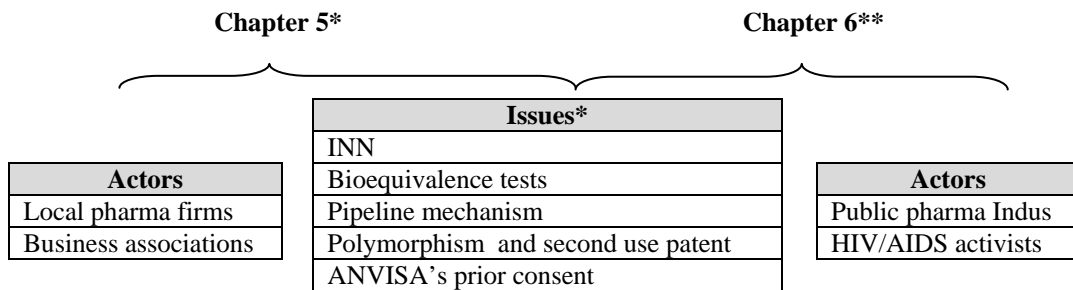


development. Because this was a period of relative stability rather than major disruptive events, I organized the analysis based on issues discussed in the pharmaceutical regulatory agenda that could influence the policy path. This included INN, bioequivalence tests and some aspects of the intellectual property law (e.g. pipeline mechanism). Because these issues were presented prior to and after the generic drug reform, it was possible to compare how an actor's meanings and understanding of them evolved in both periods. However, other concerns emerged in the agenda only in the subsequent period of reform (e.g. changes in the approval process of pharmaceutical patents) and because actors' perception of these issues could evidence aspects of their identity and policy feedback, they were included in the analysis.

For heuristic purposes and to facilitate the analysis of this period, the narratives of chapter 5 and 6 are organized according to actors/groups directly participating in the debates of these matters. Chapter 5 looks at government intervention, market demanders and suppliers. At first, it seemed intuitively plausible to assess how Serra's successor understood and promoted the generic drug regulation. Generic drug policy has been marketed as a government intervention to overcome a market failure, it would then be logical to expect that government would have a muscular role in stimulating and promoting these products to encourage demand and supply. Because government advocacy and public opinion/health professionals' support proved to be inadequate to explain the path of generic drug regulation, this chapter placed more emphasis in assessing the behaviour of local pharmaceutical producers. The AIDS activists and public pharmaceutical industries were clustered in chapter 6 as they have common issues at stake (e.g. the production of antiretroviral drugs) and carry the unforeseen policy costs, thus for clarity purposes it would be reasonable to dedicate a chapter to assess them. The analysis of preferences and demands are more complex than a dichotomous division of support vs. opposition, thus a parsimonious presentation of their behaviour is not pictured here but is assessed in detail throughout these chapters. It is relevant to note in advance that the interactions between actors were considered and highlighted when necessary. These interactions

(or the absence of them) were also assessed in the final chapter of this thesis. Figure 2 illustrates the rationale of these chapters.

**Figure 2. Illustration of Chapter 5 and 6 rationales**



Note: \*Chapter 5 begins with an analysis of government and market demand, as empirical evidence pointed that these explained less the policy legacy than local pharmaceutical firms, I weighted this chapter more on the side of local pharma firms. \*\*Chapter 6 includes issues over compulsory license and ARV drugs patent application that is not a subject of debate for the other interest groups.

## Ethical Issues

This research was assessed by the School of Social and Political Studies ethical review form for level 1, 2 and level 3 auditing and discussed with the study's supervisors. Although this study presents little risk to the individuals, it dealt with sensitive information. Sensitive information refers less to emotional distress than the consequences of the disclosure confidential communication. For example, an informant could explain persecutory actions taken to enforce a particular perspective or when explaining his/her disagreement with a particular governmental decision the respondent could use a pejorative tone to describe other participants of the policy process. The intention here is not to solve disagreements or investigate interest groups' tactics or personal motivations. For both examples mentioned, the interview process would be relevant to highlight the collective perspective of the group this respondent represented on a particular issue. Furthermore, the empirical data was indifferent with individual identities.

Several actions had been taken to guarantee ethical caution. I explained the purpose of my research to all the interviewees and gave them a brief summary of my research

and a letter from my supervisor introducing the study. Before each interview, I asked for permission to record the conversation and cite the interview. Noteworthy, I asked for verbal consent but a written consent form was prepared if the interviewee requested (no interviewee considered a written permission) (annex 3).

To ensure confidentiality, I was the only person with access to all qualitative data. Trained research assistants transcribed nearly 30% of the interviews but I excluded the name and title of the interviewee in these cases. Because some information about the respondent could be assessed in the transcription process, I was careful to explain to the assistants about the ethical implications of those conversations. All hard copy material was stored in my locker in the School of Social and Political Science, Edinburgh University, Edinburgh. Electronic material was stored on my external hard drive and password protected. Finally, when writing up the historical narrative, for the majority of interview quotes I used generic titles based on occupational and institutional position. However, for some it was necessary to reveal the respondents identity. In these cases, I made sure that the information provided was not confidential and could be found in other public sources such as newspaper articles and official documents.

Finally, I have received ethical training to conduct human subject research by John Hopkins School of Public Health, United States (computer-based module, 2002) and by Brazil's National School of Public Health in 2005. By following the aforementioned procedures, I tried to ensure a high level of ethical caution and confidentiality according to the guidelines of the University of Edinburgh Graduate School of Social and Political Science, the British Social Science Association (SRA) and the Brazilian National Commission for Ethics in Research (CONEP).

### **Institutional support & fieldwork funding**

During field research, between March and August 2009, I was hosted by Dr. Francisco Inacio Bastos at the Center for Information on Science Technology (ICICT), Oswaldo Cruz Foundation / Ministry of Health in Rio de Janeiro, Brazil.

Institutional support from FIOCRUZ increased this project's legitimacy and helped in gaining access to key-informants and exchanging information with Brazil's health policy experts. The six months of field study in Brazil was partially funded by a small project grant by the University of Edinburgh Development Trust (£1000), by the Graduate School of Social and Political Science (£260) and personal funds (£2000). These covered travelling expenses to three states in Brazil (Rio de Janeiro, Sao Paulo and the Federal District), interview transcriptions and desk research supplies.

## **Conclusion**

This chapter discussed the research protocol for this thesis, taking into account the theoretical parameters presented in Chapter 2. Historical institutional analysis requires a longitudinal approach to the policy process, which in turn is better assessed through process tracing analysis and qualitative research methods. This chapter also discussed the options for the Brazilian case study and the parameters and dilemmas to assess policy preference. An in-depth description of the methods used (documentary research, elite interviews and quantitative data) illustrated how the empirical material was collected and its relevance to assess the policy process of generic drug regulation in Brazil but also how it was organized to inform the analysis of this thesis. This chapter ended by providing the rationale of data analysis and the organization of the empirical chapters. It also explored the research practicalities (e.g. institutional support) and the ethical considerations.

## **4. The generic drug reform in Brazil**

This chapter traces the deliberation process of Brazil's generic drug regulation, that is, the critical period of reform and its institutional antecedents. The first part provides historical background information about the local production of medicines and is important in order to contextualise the pharmaceutical sector in Brazil. The second part of this chapter assesses the three antecedent events to the Generic Drug Act that happened to come together in the 1990s: the initial attempts to introduce a generic drug regulation in Brazil, the enactment of intellectual property law, and the HIV/AIDS epidemic. Tracing these events helps in identifying the circumstances that led to this regulatory reform, the participants of the pharmaceutical sector, their preferences and demands. The third part of this chapter deals with the critical period of generic drug reform between 1999 and 2002. It presents the contingent events that led up to the crisis in the pharmaceutical sector and thus triggering this regulatory transformation, and the political entrepreneurship of the Minister of Health, who used the opportunity to implement his ambitious regulatory agenda. This third section is divided into two parts for clarity purposes. First, it deals with the parliamentary bargain to enact the Generic Drug Act in 1999 and, second, assesses the Ministry of Health and the Health Surveillance Agency efforts to put this legislation into practice (e.g. political activity and policy instruments to induce supply and demand of generic drug products).

### **Background: local production of medicines**

Brazil has a long tradition of local production of medicines, both private and public (Saraiva 1983; Bermudez 1992). Although, during the 1940s, scientific advances made possible the discovery of antibacterial medicines and others chemical syntheses (cf. Achilladelis and Antonakis 2001), local industries in Brazil lacked the technology to follow the pace of pharmaceutical research and development in the US and Europe (Saraiva 1983). It was only after World War II that Brazil began its industrialisation process, based on a model of Import-Substitution Industrialisation

(ISI), which involves stimulating local production by increasing barriers to import products (Baer 1972)<sup>32</sup>. ISI would protect the pharmaceutical market from international competition, whilst encouraging multinational pharmaceutical firms to bring their research and development activities to Brazil (as imports were forbidden they would have to establish subsidiaries and produce drugs locally and, arguable, this could in the medium-long term transfer technology to Brazil) (*ibid*).

However, the ISI was not sufficient to contain the accelerated process of denationalisation in the pharmaceutical sector, that is, the increasing movement of multinational industries into the Brazilian market. Scholars suggest that monetary policies adopted during this time opened sectors of the Brazilian economy to foreign capital, including pharmaceuticals (Caputo 2007). For instance, the Instruction 70/1953” and “Instruction 113/1955”<sup>33</sup> provided favourable exchange rates for firms importing capital goods to establish new factories in Brazil (Nucleos de Estudos Politicos e Sociais / ENSP / Fiocruz 1991; Sindusfarma 2006; Caputo 2007). On the other hand, other scholars suggest this has less to do with monetary policies than with the technological development of the sector itself and the local firms’ incapacity to catch up with their foreign competitors (Evans 1979). Nevertheless, for the purpose of this study it is important to understand that, by the end of the 1960s, multinationals had stepped foot in Brazil and managed to capture the majority of the Brazilian market by acquiring local industries and installing subsidiaries.

Dissatisfied with the denationalisation of the pharmaceutical sector and with the limited research and development capacity of local firms, the Brazilian government decided to abolish patent protection for pharmaceuticals (Cassier and Correa 2003: 92-93)<sup>34</sup>. Brazil is a signatory of the 1883 Paris Convention that regulates intellectual property rights (revised in 1963 in Stockholm). However, in 1945 President Vargas decided to exclude patent protection for pharmaceuticals (Tachinardi 1993) and, in

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<sup>32</sup> Until then, Brazil and other Latin American countries were basically exporting food and raw material to Europe and United States while exporting industrialised goods (for more detailed information of ISI model see Baer 1972).

<sup>33</sup> This was an exchange rate policy that had an impact on the industrialisation process in Brazil. For a comprehensive analysis of the impact of this decision see the study of Caputo (2007).

<sup>34</sup> However, it is arguable that lack of patent protection could foster technological development in Brazil as it also reduced incentives for research and development (cf. Evans 1979: 186).

1969, President Costa e Silva excluded patent protection of the pharmaceutical process. Both decisions were reassured in 1971 with the Code of Intellectual Property, under the Medici administration (*ibid*). On the other hand, public investments to foster the production of fine chemicals in Brazil were very fragmented (Leite 2008)<sup>35</sup>. Despite the fact that Brazil did not have a code of intellectual property rights, research-based firms continued expanding their business in Brazil (Tachinardi 1993: 73).

A study made by Peter Evens (1979) on the industrialisation process in Brazil suggests that Brazilian firms survived through this adverse period of denationalisation by using their commercial acumen:

They [local pharmaceutical firms] make no pretence of trying to develop “original” products and are perfectly willing to admit that their product lines consist of “similar”, that is, products originally developed by other companies. To say that local entrepreneurs have come to rely on their commercial ability rather than on technological competition is hardly to condemn them. They have discovered where their “comparative advantage” lies [...]. That they continue to survive in an industry where so much militates against their survival is proof of their skill (Evens 1979: 128-129).

In other words, Brazilian firms were not competing at the technological level, but there was an acute competition for market share. In 1969, foreign firms represented 82% of the market share in sales compared to 18% for Brazilian firms (Sindusfarma 2006). In order to survive in this unfavourable scenario, local firms began aggressive commercial strategies. Some common terms in the pharmaceutical sector in Brazil are the “bonus sale”, that is, price discounts for drug retailers that ‘pushed’ similar pharmaceutical products to consumers – particularly those seeking medicines without medical prescriptions<sup>36</sup> (Saraiva 1983). Brazilian pharmaceutical firms then became an industry of “similar pharmaceutical products”. Note that these are not generic drugs, as there was no discussion about bioequivalence and this term was not on the

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<sup>35</sup> For example, the agency *Companhia de Desenvolvimento Tecnológico* (CODETC), a state enterprise created in 1976 that intended to replicate the manufacturing process of innovator medicines, serve as business incubator providing technical support to firms interested in chemical synthesis of pharmaceuticals etc. The study of Leite (2008) suggests that this project did not last long due to changes in government priorities.

<sup>36</sup> Self-medication has been a long public health concern in Brazil and this cultural (and market) aspect favoured these commercial practices. Anecdotal evidence suggests that these are practices adopted not just by local firms but also by many multinational companies. Because these are detailed aspects of marketing strategies, I did not focus too much on them.

agenda. Similar pharmaceutical products were recognised for the first time in Brazil in 1979, after Congress approved a legislation regulating these products (Sindusfarma 2003: 55). Thus, the absence of patent protection and a similar drug regulatory framework allowed local pharmaceutical firms to legally replicate any product without payment of royalties and expand their industrial production. Regulatory concerns of government officials at that moment were less about the technical requirements to register a pharmaceutical product than bidding and labelling requirements introduced with this legislation<sup>37</sup> (Sindusfarma 2003).

In summary, this brief contextual information suggests the pharmaceutical sector in Brazil was highly unregulated as there was no intellectual property protection and very limited and insufficient health surveillance. Additionally, the pharmaceutical sector was highly competitive at the final stages of the production chain; in other words, because local firms had limited research and development capacity, competition centred on marketing strategies. However, Brazil's political context changed substantially by the end of the 1980s with the redemocratisation process after 20 years of military regime and the approval of a new Constitution in 1988. It was during this period that the generic drug regulation and several other important pharmaceutical regulatory decisions were taken. These reforms are examined in the following sections.

### **Institutional antecedents**

This section explores three events antecedent to Brazil's generic drug policy: 1) the unsuccessful attempt to introduce generic drugs in 1993; 2) the approval of a patent act in 1996; 3) the rise of the HIV/AIDS epidemic and the legislation guaranteeing universal treatment to AIDS patients in 1996. Although the policy process of each of these events occurred relatively independently, the fact that they happened to come together in the 1990s had a profound relevance to the decision to introduce a generic

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<sup>37</sup> For example, Law 6063/76 requires that all prescription drugs commercialised in Brazil must provide a red tape indicating that the medication should only be sold with medical prescription. This norm received many complaints from the pharmaceutical firms due to the cost associated with it.



drug regulation in 1999. I will focus in this section on how political actors interpreted each of these streams, which conditioned their position in the generic reform in 1998.

### **Early attempts to introduce Generic drugs**

A new Constitution was approved in 1988 and established the legal basis for a universal health care system. Under this new institutional context, the government was to provide universal pharmaceutical assistance to all Brazilian citizens. The guidelines to do so were slowly developed in the 1990s (Levcovitz et al. 2001). However, concerned with increasing pharmaceutical expenditure and the population's deficient access to medicines, the Federal Deputy Eduardo Jorge presented a bill to regulate the market for medicines in Brazil in 1991 (Bill 2022/1991). Jorge was a physician and former director of the Municipal Health Secretariat in 1989. It was during his tenure at the Secretariat that he became aware of the relevance of pharmaceuticals to the government's health budget and the suggestions of the World Health Organization to introduce generic drugs (Jorge 2009). The rationality of this project was that, by excluding the brand name of pharmaceutical products, it would lower its cost. It argued that:

Competition in pharmaceutical sector demands high efforts to promote brand names that differentiate products. The promotion of these brand names takes around 20 to 30% of gross revenue of pharmaceutical firms. This expensive promotion aims to capture credibility of doctors, patients and pharmacists etc" (Bill 2022/1991).

Justified by the fact that 50 million people had limited access to medicines, the bill proposed that all pharmaceutical products in Brazil should be commercialised using either the Brazilian or International Non-proprietary Name (Law Project 2022/1991). The use of brand names would be allowed only if presented in a lower size compared to the generic name; all public health service prescriptions should be done by the generic name (*ibid*). However, little attention was given to this bill, perhaps because the weight of the pharmaceutical sector attention was focused on another highly controversial debate that was taking place at the same time, namely the introduction of a patent system (which will be presented in the following section).

Discussions on generic drug gained visibility in 1993. With the deregulation of price control of medicines in 1992, some drugs were readjusted by more than 2.600% while annual inflation rates were 1.608%<sup>38</sup> (Abbas and Bermudez 1993; Bermudez 1999). It was estimated that 50% of the population had no access to medicines (ALANAC 2010). The higher costs of medicines were constantly criticised by the media, demanding a prompt governmental response, which placed access to medicines at the top of the agenda (Folha de Sao Paulo 1993). After President Collor resigned in 1992, his substitute, Itamar Franco (1992-1995), brought Jamil Haddad into the Ministry of Health. Haddad, a physician with long involvement with the sanitary movement, was also a Federal Deputy and participated in the debates of the Bill 2022/1991 to regulate generic medicines in the Chamber of Deputies, Social Security Committee (Haddad 2009). Under Haddad's leadership, the Ministry of Health first endorsed the regulation of generic medicines, following the guidelines of the World Health Organization:

I had just received a letter from the WHO and they stated the urgent necessity to implement a generic medicine plan, particularly because of the low income condition of the population. [The Federal Deputy] Eduardo Jorge, in 1992 [...] had also received this document from the WHO and introduced a project on generic medicine. [...] When I became Minister I verified that project was in the Congress drawers due to laboratory's pressure. My juridical assistant told me it didn't need to be implemented by law but it could also be by presidential decree (Haddad 2009).

This information highlights how decision-makers in Brazil first became aware of the necessity of a generic drug policy. In April 1993, the Ministry of Health sponsored an International Seminar to discuss different experiences of developing a generic drug policy. It invited advisors from the Pan-American Health Organization, academics and health policy experts from Canada and other countries that implemented generic drug regulation (Arango 1993; Velásquez 1993). Following this event, President Itamar Franco issued a presidential decree (793/1993) introducing generic drugs in Brazil. Although proposals presented during the seminar highlighted the relevance of technical requirements to implement generic drugs, for example bioequivalence and bioavailability tests that are considered by the WHO guidelines, the Presidential Decree did not mention these specifications. It was not possible to

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<sup>38</sup> Note that at that time Brazil had extremely high annual inflation rates.

assess exactly why Itamar Franco and Jamil Haddad decided to ignore this aspect of the WHO prescription. The presidential decree 793/1993 would require a complex reorganisation of the pharmaceutical sector as it mandated that: the brand name could not exceed 1/3 of the generic name; drug retailers should present a list of generic medicine names; every institution that manipulates medicines should have a pharmacist; all drugs prescribed and procured by the National Health System should use the generic name.

The pharmaceutical industries and drug retailers promptly reacted, triggering a political process that was beyond the WHO decision or influence and mediated by domestic institutions. Alteration in labels of pharmaceutical products would bring economic distress to both national and multinational companies. Most ‘similar drugs’ in Brazil had also held a brand name. It would then require costly readjustment in packing and marketing strategies. A debate sponsored by the newspaper *Estado de Sao Paulo* brought together representatives of the pharmaceutical sector, government and health professionals. The local industry expressed its concerns: “as a Brazilian industrialist I felt deeply harmed. I could never expect that a product I brought to the market, that prescribed by doctors -- with a brand/trademark -- would be annihilated by a Decree” said Omilton Visconde (Visconde in Estado de Sao Paulo 1993a: A24). Although bioequivalence criteria was little debated at that time, the President of Abifarma, Jose Eduardo Bandeira de Mello, explained his disagreement:

Our core objection to this Decree is that it ignores the basic requirement of generic drugs that was adopted by other countries and by the World Health Organization, which is quality. Quality can only be assured under a rigid supervision and requires that generic products must provide bioequivalence and bioavailability tests. The Decree ignores this aspect [...] (Mello in Estado de Sao Paulo 1993a: A24)

According to an executive of a multinational pharmaceutical firm that participated in this debate, a core objection of multinationals was the absence of patent protection rather than generic drugs themselves: “If you create the classic generic, with bioequivalence and bioavailability, and do not create a patent system, then what you are doing is a license to copy” (Sanchez 2009). Clearly, the regulation of off-patent pharmaceutical products was not the priority of pharmaceutical firms. For

multinationals, the introduction of a patent system was imperative; only after granting intellectual property rights would it be reasonable to debate generic substitution. Their counter-demand did not include bioequivalence or alteration in labelling; rather, they proposed a basket of medicines with price discounts for institutional purchase (Abifarma 1997a).

Furthermore, the decree also brought opposition from drug retailers' representatives as it mandated the presence of pharmacists in each pharmacy around the country, increasing their business costs. Drug retailers joined pharmaceutical firms in being discontented with this political decision (Estado de Sao Paulo 1993c). There was a joint initiative in the pharmaceutical sector to block the decree's implementation. With the Legislative and Executive being less sensitive to their demands, the coalition of firms and drug retailers used judicial trials to block the decree's implementation. Abifarma and Sindusfarma used courts to complain against the decree. Additionally, 22 pharmaceutical industries and drug retailers introduced law suits individually (Visconde in Estado de Sao Paulo 1993: A18; Gazeta Mercantil 1993; Jornal de Brasilia 1993; Gazeta Mercantil 1993a; Estado de Sao Paulo 1993b). As the judicial battle between the executive government and Abifarma slowly evolved in the courts, pharmaceutical firms and drug retailers could delay the introduction of generic drugs.

On 5 October 1993, *O Globo*, Brazil's largest newspaper, reported that "without the support of the pharmaceutical industry, pharmacies will open, ignoring the law requirement to provide generic names for all medicine bids and labels" (O Globo 1993) (see also: Jornal do Brasil 1993a). To further complicate matters, the demand (namely by doctors, consumers, pharmacists) was unconfident of the quality of drugs commercialised by the generic name or even unaware of the debate (Costa and Hojaij 1993; Estado de Sao Paulo 1993; Rabaca 1993; Estado de Sao Paulo 1993a).

Together with the tense relationship with the private sector and being faced with a delay to bring generic drugs to the market, the new Minister of Health, Henrique Santillo (1993-1995), decided to reconsider the size of INN in labels. In contrast,

Abifarma proposed a basket of medicines with a 50% discount in price and a 150-day grace period for the private sector in which to adjust its products (Jornal do Brasil 1993; Jornal de Brasilia 1994a). As no political consensus could be reached, courts would have to rule on this issue (Correio Braziliense 1994; Jornal de Brasilia 1994).

Why, despite the World Health Organization's recommendation to introduce generic drugs, did the Brazilian Congress and the Ministry of Health fail to persuade pharmaceutical firms (local and multinational) and drug stores to commercialise products by their International Non-proprietary Name? The failure to implement the Decree 793/1993 is associated with different factors. First, the lack of support by the pharmaceutical sector suppliers, both firms and retailers, certainly matter the most as a result of the failure of the Decree. But also lack of support from consumers and health professionals harmed the introduction of the Decree as they could not fully understand the discussion or were unsure of the quality/safety of generic medicines. Some argue that generic drugs were not safe/efficient as innovator drugs, while physicians had little knowledge about the INN. Second, it is also argued that the Ministry of Health was unable to enforce the regulation; for example, the Department of Sanitary Surveillance was unaware of the number of pharmaceutical industries established in Brazil. More importantly for this study is the fact that pharmaceutical firms, particularly the local producers, were eager to defend their economic stakes, i.e. the trademarks.

Third, and perhaps mostly importantly, it highlights that local pharmaceutical firms were starkly opposed to the attempt to exclude their trademarks and commercialise their products by a BNN or INN. In this period of confrontation with government, it is possible to visualise the preferences and demands of the firms. Looking at this particular point in time it could be argued that pharmaceutical firms (national and multinationals) behaved strategically, making rational calculations to protect their economic interests. In this sense, the regulatory policy proposed by the government had little influence in their business. A study conducted in 1998 with a non-representative sample demonstrated that pharmaceutical manufacturers did not

comply with Decree 793 requirements (Pizzol et al. 1998), particularly in relation to the obligation to the size of brand and generic names; for example, it was found that, for some drugs, brand name was 16 to 20 times larger than the INN. Thus, little has changed in the behaviour of these firms.

### **Patent system reform: Bill 824/1991 and Law 9279/1996**

As seen in the background information for this chapter, since 1945 Brazil did not recognise pharmaceutical patents. In the late 1970s, pharmaceutical industries (and other high-technology sectors) in the United States began voicing the fact that their products were facing competition in foreign markets that did not protect intellectual inventions (cf. Weissman 1996; Sell 2002). In 1988, the United States Pharmaceutical Manufacturers Association (now Pharmaceutical Research and Manufacturers of America - PhRMA) filed a complaint with the United States Trade Representative (USTR) about Brazil's lack of process and patent protection for pharmaceutical products. In response, on 30 October 1988, the United States government, under the Reagan administration, imposed a punitive tariff of 100% on US\$390 million worth of Brazilian goods (penicillin and tetracycline, paper and cellulose, among other products) (Revista Veja 1991; Revista Veja 1993). This was in retaliation for Brazil's refusal to grant patent protection to pharmaceuticals, and other information-intensive technologies (*ibid*).

These sanctions were suspended in 1990 after a visit from the American President George Bush, when the Brazilian government announced its intention to submit a bill for intellectual property rights (Feghali 1991; Forum pela liberdade do uso do conhecimento 1994; Pharmaceutical Business 2000). Note that these events were happening parallel to the discussion of generic drug regulation, but are separated here for clarity. The recently elected President Fernando Collor de Mello (1990-1992) was willing to integrate Brazil with the global economy and thus sensitive to intellectual property issues. On 30 April 1991, he sent a bill to Congress requesting its urgent appreciation (Bill 824/1991) (Forum pela liberdade do uso do conhecimento 1994: 11). Furthermore, in 1991, Brazil hosted the 11<sup>th</sup> International Seminar on Industrial Property, which placed the country at the centre of its

discussions (Revista Veja 1991). This brought even more media coverage and political attention to this issue. Debate around IP is historically divided into two periods: firstly in 1991, when Collor first presented the legislation in Congress, but discussion was suspended due to the political moment (corruption scandal that led to the President's impeachment); in the second period, the debate was resumed in 1996 under the Cardoso administration and following the General Agreement on Tariff and Trade – the GATT agreement.

Scholars of international relations have analysed the American firms' (and, later on, European and Japanese firms) crusade to harmonise international IP regulation (cf. Sell 1995; Sell 2002; Sell and Prakash 2004). Sell and Prakash (2004) provide a comprehensive analysis of the agenda setting and the IP coalition that drove the discussions from the World Intellectual Property Organization (WIPO) to the General Agreement on Tariff and Trade (GATT), leading to the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) in 1994. The authors suggest that a coalition of developed countries and research-based firms successfully managed to frame the debate of patent protection as an issue of technological and economic development. They suggest that the coalition's key framing strategy was the assertion that property rights were being illegally appropriated by pirates.

An alliance of foreign firms, the executive government and the American government representatives represented the pro-IP coalition in Brazil. The discourse of Brazilian federal government and multinational firms was framed in ethical values and economic development. The pro-IP coalition declined any allegation of foreign pressure, arguing that the debate was a matter of local interests (Teixeira 1991):

Of course we cannot exclude the international aspects of this issue. Any person with an impartial vision of this issue could not decline the rights of researcher and their sponsors to defend themselves from predatory action of copiers or imitators; which steal from them and their governments the gains of their research and investment. [...] It is estimated that 20 million dollars are invested in pharmaceutical research worldwide. Nowadays Brazil represents 2% of pharmaceutical market, it is reasonable to assume that we will have the same proportion of investments – which would lead multinationals to invest around 400 million dollars in pharmaceutical research in Brazil. Almost half of what Brazilian government invest in all its research areas [The executive president of the Brazilian Association of Research-based Pharmaceutical Industry] (Teixeira 1991: 9).

The discourse of Teixeira represented the interests of Interfarma (association of research-based pharmaceutical firms) and balances the arguments of foreign pressure to introduce patent protection in Brazil with the domestic interest of the country. In other words, his claim is that the government could reap similar benefits in terms of economic development, placing Brazil at a different stage of technological development. Additionally, his discourse included normative values, as the ethics of copying a product invented by other firms without permission. In 1991, he declared: “Brazil is copy-paradise. It is possible to copy anything here without paying [royalties to] the inventor” (Teixeira in Revista Veja 1991: 95). Interfarma was created in 1990 to represent the interests of research-based firms, mostly foreign companies. There was an agreement between pharmaceutical firms that Abifarma and Sindusfarma, other pharmaceutical firms’ association, would not get involved in IP debates given that its members were both foreign and international firms (Mello 2000; Sindusfarma 2006). While research-based firms’ preferences were represented by Interfarma, local firms’ interests were represented by Alanac (*ibid*).

Unlike the international debate where the business network did not encounter significant NGO mobilisation (Sell and Prakash 2004), the domestic discussion around intellectual property faced strong opposition. Sell and Prakash (2004) argue that, during the TRIPS negotiation, there was no significant challenges from a competing NGO-inspired normative frame, leaving an open path for businesses to graft their agenda onto policy debates. In Brazil, the anti-IP coalition was formed by local pharmaceutical industries (represented by Alanac), different sectoral interests (e.g. chemical engineers, syndicate of pharmacists) the Catholic Church and leftist politicians [Worker’s Party (PT), a segment of the Brazilian Democratic Movement Party (PMDB) and the Brazilian Communist Party (PC do B)]. This coalition was organised in the Forum for Free Use of Knowledge (*Forum pela Liberdade do Uso do Conhecimento* (FLUC)) with more than 80 institutions (Forum pela liberdade do uso do conhecimento 1994: 12)<sup>39</sup>. It defended “anti-denationalisation” values, access to essential medicines and the protection of local biodiversity. Among these, access

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<sup>39</sup> Note that the HIV/AIDS NGOs were not engaged in regulatory or trade debates in the 1990s. As we shall see in the following section, its demands focussed on access to medicines and they were less aware of the implications of intellectual property or generic regulation at that time.



to essential medicines was a topic supported mainly by Alanac, academics and leftist politicians. The local pharmaceutical industry defended the status quo of the IP code, arguing that absence of protection would give Brazil more time to develop its local industry:

[...] if this law is enacted foreign laboratories won't have to face competition. A monopoly will be established and we need to accept the prices they determine [...] Congress is placing health sector in the hands of multinationals. However, in Brazil and in Latin America, there is Chagas disease for example. These diseases won't be researched because the market is small and they won't research such restricted segment. [...] How to design a health policy with the whole sector driven by multinationals? They say out and loud: medicines are for those who can afford, and we, from Alanac, do not agree that this should be the tone of medicine's issue in Brazil [Dante Alario, President of Alanac] (Alario in Forum pela liberdade do uso do conhecimento 1994: 22).

The discourse of Alanac demonstrates local pharmaceutical firms' preference to remain an industry of similar products. However, the claim in Alario's speech is not to maximise the profits of his members, rather it is concerned with the future of neglected disease research and development and the formulation of Brazil's health policy in the context of price monopoly. The coalition prepared two reports, or "Patent Dossier", presenting the critical points of the patent legislation and its demands (Forum pela liberdade do uso do conhecimento 1994). Among the 15 critical points presented were two particularly harmful to the local pharmaceutical industries: first, article 18 of the IP bill listed products exempt of patent, where the coalition required that all drugs presented in the National List of Essential Medicines (around 300 medicines) should also be listed as patent exempted; secondly, they also demanded the exclusion of article 241 of the bill, which misleadingly linked the issue of industrial protection with sanitary surveillance. This article would invalidate Law 6063/1976 that regulates similar drugs in Brazil. This reinforces, once more, the fact that the preferences and demands of local pharmaceutical firms were to protect their rights to produce similar drug products.

Because of the political climate and the impeachment of President Collor, the discussion on patent protection was suspended and then resumed in 1995. While internal debates in 1993 and 1994 in the pharmaceutical sector were turned to the introduction of generic drugs (presidential decree previously discussed), at the

international level, the pharmaceutical sector was focused on the Uruguay Trade Round, which concluded in December 1993. The final GATT round created the World Trade Organization (WTO) and established minimum parameters for intellectual property rights under the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS)<sup>40</sup>. Although there was an intense debate around the inclusion of intellectual property on trade agreements, the Brazilian delegation headed by Chancellor Luis Felipe Lampreia agreed to sign up TRIPS if there was a separate discussion for tariffs (Lampreia 1995c). Brazil quickly ratified the Uruguay Trade Round agreements in that same year and its negotiations were concluded (Legislative Decree 30/1994 and Presidential Decree 1355/1994) and, by doing so, it committed to revise its intellectual property code.

The election of President Fernando Henrique Cardoso in 1994 opened a window of opportunity to bring intellectual property back onto the agenda. Cardoso served as a Minister of Foreign Affairs under President Itamar Franco (1992-1993) when he coordinated an Interministerial Group to debate intellectual property issues. He also served as a Minister of Finance (1993-1994) responsible for introducing the *Plano Real* (Real Plan) that controlled hyperinflation and stabilised the economy. Had FHC lost the presidential election to the leftist Luis Inacio Lula da Silva, the chances of opening Brazil's economy to foreign investments might have been lower. Cardoso was interested in boosting Brazilian credibility with foreign investors; however, in order to do so, he would need to introduce several reforms, including modernising Brazil's patent system, and he could not ignore international trade obligations (Lampreia 1996a; Lampreia 1999: 286). There was a strong effort from the executive government to push the patent legislation in Congress:

“We need to fight plagiarism. Refusing to recognize patents is consolidating the pirates” said the minister Jose Israel Vargas (Science and Technology). According to the ministry, in 1970 Brazil participated with 2% in pharmaceutical sector worldwide. In the beginning of the 80s, it fell to 1.8% and reached 0.2% in the early 90s. “The lack of intellectual property did not contribute in anything to increase industry's potential. We hope to reverse this with law's enactment” said Vargas (Folha de Sao Paulo 1997).

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<sup>40</sup> All middle income country members of the WTO would have to implement TRIPS by 2005, while least-developed countries by 2016.

Together, the Minister of Science and Technology (Israel Vargas), Minister of Foreign Affairs (Luis Felipe Lampreia) and the Vice-President (Marco Maciel) lobbied Brazilian Congressmen between 1995 and 1996 to approve the legislation (Folha de Sao Paulo 1995; 1996; 1996b; 1997). They tried to discredit arguments of denationalisation by counter-arguing that, although Brazil did not have patent protection for so long, it was not enough to encourage local technical development. With the approval of the Trade-related Aspects of Intellectual Property Rights (TRIPS agreement), the American government intensified its support for patent reform in Brazil. In March 1996, the Counsellor to the US President, Thomas McLarty, declared:

We did discuss that with President Cardoso, who is quite optimistic and hopeful that it will be passed in the House [referring to the final round of debates in Congress]. It is important not only for the United States and interests there, but it is important from Brazil's standpoint in terms of attracting investment to this country. And foreign investment have been on a very strong pace here in recent months (McLarty in McLarty and Watson 1996).

The debates in Congress were polarised between Senator Ney Lopes supporting the pro-IP coalition versus Senator Ney Suassuna and Senator Jose Sarney (former President from 1985-1990) supporting the anti-IP coalition. Essentially, there were four points of disagreements between them (Folha de Sao Paulo 1996c): (1) pipeline patents, whether or not to allow retroactive patent protection of products not commercialised in Brazil; (2) biotechnology, which would allow the patent of micro-organisms used in biotechnological products or restrict those genetically modified; (3) production, whether or not to allow multinationals to import patent products or require these firms to produce patent products in Brazil; (4) grace period, whether or not to use the 5-year grace period allowed in TRIPS. One of the most polemic issues was the pipeline mechanism, which allows retroactively patent products that have been previously patented in other countries. This would limit the number of products national firms were allowed to copy and would require royalty payments if they decided to do so.

The pipeline mechanism was an amendment proposed by Senator Fernando Bezerra to the intellectual property bill in 1991 (Folha de Sao Paulo 1996c). Surprisingly, Senator Bezerra was also president of the National Confederation of Industries

(CNI), which raised deep criticism from local pharmaceutical industries and other nationalist groups: “It is shameful that the president of CNI says he represents the national industry. What he defends is the sector of international firms’ members of CNI. We do not consider ourselves represented by him” said Dante Alario, president of Alanac (Alario in Folha de Sao Paulo 1996a). The anti-IP coalition argued that patent protection would create a “monopoly of cure”, claiming that many Brazilians would not be able to afford expensive patent medicines. Moreover, they supported that “having its own developed industry is a question of national sovereignty for any nation” (Alario 1995). Responsible for preparing the patent legislation in Senate, Senator Ney Suassuna commented on the different lobbying pressures:

I was pressured by all sides. First, the left represented by nationalist syndicates, demanding that no patent should be recognized. And there was the Church, representatives of agriculture, government, embassies, foreign laboratories, anyway, around 150 institutions. Alanac (Brazilian Association of National Pharmaceutical Laboratories), for example, was one of the most active nationalist entities. (...) International laboratories wanted, for example, that the law, in Brazil, recognize patent of other countries but not yet commercialized here (called pipeline patent) (Suassuna's interview in Folha de Sao Paulo 1995a).

After the strong influence and pressure of President Fernando Henrique Cardoso and Vice-President Marco Maciel, the Brazilian Congress approved the patent law in April 1996 (cf. Folha de Sao Paulo 1996d). Brazil's new patent law took full effect in May of 1997. It not only just complied with the WTO international regulation but also included protections beyond TRIPS requirements: the pipeline mechanism, which granted retroactive patent protection for medicines registered outside Brazil and not yet commercialised in the country, and declined the nine years grace period allowed under the international agreement (Law 92879/1996) (these extra provisions beyond the WTO requirements are known as TRIPS-Plus).

The debate around IP protection is important for this study for several reasons. First, it is possible to observe the preferences and demands of local pharmaceutical companies in trying to defend their stakes on the rights to replicate innovative medicines. Their arguments of local production of medicines were grounded on nationalist sentiment and counter-reacted to the government agenda by saying patents would represent a “monopoly of cure”. In this sense, they argued that actors

behaved entirely strategically as to maximise their economic stances would rule out this important aspect of their preferences. The inner motivation of each of these sides is not accessible for empirical observation and that they were trying to maximise their economic interest would be inaccurate. The Brazilian government was sensitive to the idea that a protection of intellectual property was necessary and the arguments of innovator pharmaceutical firms were welcomed, as opposed to the local firms that were framed as “pirates”. Thus, it left less room for persuasive counter-arguments. Second, with the introduction of an intellectual property legislation, it was expected to marginalise even more the performance of local pharmaceutical firms as it banned them from replicating medicines developed by innovator pharmaceutical companies. While multinational firms would have their recent products protected by patent, local firms would have their production restricted to medicines produced prior to 1997. Immediate market competition would be restricted to relatively unfashionable medicines. With the introduction of the patent system for pharmaceuticals, the presence of foreign capital in this sector would expand significantly. For instance, according to Abifarma (1997), the pharmaceutical sector invested, between 1992 and 1997, around \$1.3 billion dollars in Brazil, representing one of the tenth largest pharma-markets worldwide. Foreign firms decided to place Brazil as an exporting platform to Latin America, Europe and North American. While the Europeans decided to establish manufacturing plants in Brazil, aiming at the Latin American market, the Americans believed that manufacturing products in Brazil would open the European market through the Mercosur and EU trade agreements (Mello 2000).

### **The HIV/AIDS activism**

Finally, the third event that might have channelled the generic drug regulation is the HIV/AIDS epidemic. The relevance of investigating this event is two-fold. The first is because Brazil is well-known for its remarkable AIDS advocacy, and this has been the object of many studies (cf. Galvao 2000; Galvão 2002b; Galvao 2005; Biehl 2007). As the literature review for this thesis suggested, patient advocacy activity can provide important input to pharmaceutical regulatory policies and had been said that AIDS activists championed important regulatory reforms in the American FDA at

this period (cf. Carpenter 2004). Thus, I decided to investigate in which ways the AIDS activism might have contributed to the generic drug reform. Second, Brazil is also well-known for being the first developing country to provide free and universal access to antiretroviral drugs and its intense price negotiation with multinational pharmaceutical firms to lower the costs of medicines (cf. Cohen and Dan 2003; Cohen and Lybecker 2005; Nunn et al. 2007). It is also relevant to understand in which ways this contributed or not to the generic drug regulation. There are a number of in-depth studies on HIV/AIDS policy in Brazil, consequently this section relied mostly on literature review, cross-checking this information with original interviews with AIDS activists when necessary.

Parallel to the debate on generic drugs and intellectual property, the HIV/AIDS epidemic raised much media attention in the early 1980s. The fact that the epidemic was initially concentrated in urban areas, upper middle class and cases among artists and celebrities, contributed to give visibility to the disease (cf. Parker 1987). The cost of the first drug to treat AIDS patients (zidovudine) was prohibitive for many Brazilians (around \$8.000/year) and the recent established Unified Health System was unprepared to deal with this sudden demand (cf. Nunn 2008: 49). People living with HIV/AIDS (PLWHA) began to organise themselves into local and regional associations, demanding a prompt response from the government. Several studies reported that these AIDS activists voiced their dissatisfaction in the judiciary (Galvao 2005; Scheffer et al. 2005; Nunn 2008)<sup>41</sup>: “The judges often ruled favourably, citing Brazil's constitution, which guaranteed that every citizen had a right to health and the state had a duty to ensure every citizen's health” (Galvao 2005: 1112). The demands of activists, which focused on anti-discrimination initiatives and gaining access to medical treatment, was framed in a discourse of human rights and to democratic access to health treatment (Galvão 2002b; Galvao 2005; Nunn 2008: 50-51). According to Nunn (2008: 50-51), human rights were an overarching frame for this activism, political actions and slogans. The “rights” language would not just shift the

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<sup>41</sup> Scheffer, Salazar *et al.* (2005) provides an extensive review of the story of the HIV/AIDS judicial cases, and analysis of the jurisprudence and its outcomes, while Nunn (2008) analyses the strategy of NGOs to forum shop and pressure for a governmental response.

stigma of “victim” away from these patients but would also legally justify their demands within the Constitutional right to health care to all citizens.

The literature on AIDS policy in Brazil suggests that, in the early 1990s, the relation between activists and government was conflicted, particularly during the short administration of President Fernando Collor de Mello (1991-1993) (Parker 1994; Galvao 2000; Nunn 2008). The study of Nunn (2008) on the history and politics of AIDS treatment in Brazil demonstrated that it was in this period that the federal government formally committed to provide zidovudine to AIDS patients. However, there was an irregular supply of these medicines because of the fragmented health infrastructure and limited health sector budget. Nunn points out that the conflicting relation between activists and the government resulted from the fact that the Department of AIDS was less sensitive to the human rights discourse and had limited dialogue with the NGOs. During this period, its director was the physician and professor, Eduardo Cortes. He adopted a pragmatic approach to the epidemic and human rights were not the tone of his decision making. It was during Cortes' tenure that Brazil initiated conversations to contract a World Bank loan to develop a national strategy in order to control the HIV epidemic (Nunn 2008: 54-55).

Nunn suggests that confrontation between government and activists lasted for a short while and the dialogue was re-established in 1993, after Cortes left the government. The former director of the Department of HIV/AIDS, Lair Guerra, reassumed the post and continued the discussions with the World Bank. Besides helping to build up an impressive response to the epidemic, this foreign aid had sweeping effects on the HIV/AIDS activism by financially supporting and empowering these groups. Representatives of civil society and health professionals helped in the design of the World Bank loan agreement and later on many of these were invited to join the National Coordination of HIV/AIDS as staff members (Nunn 2008: 61). This gave them an advantageous position to participate in the development of Brazil's response. The loan agreement included funding for NGO projects ranging from capacity building, advocacy events (e.g. the annual gay parade in Sao Paulo), to preventive interventions with vulnerable population (cf. Fonseca et al. 2007).

Although this resource might have fostered the vibrant AIDS advocacy in Brazil, it also received much criticism from NGOs insiders for silencing their militancy. The dissatisfaction of some activists with this new role of HIV/AIDS NGOs was reported by Joao Biehl (Biehl 2004) in his book *Will to live: AIDS therapies and the politics of survival*. In chapter two of this ethnographic analysis of the Brazilian response to the HIV/AIDS epidemic, the author provides rich evidence of several activists being frustrated – not with the government response – but with the “industrialization of nongovernmental work” and “depoliticized mission of NGOs” (pages 106 and 112, respectively). These activists’ concerns were that the close collaboration with government reduced their street and juridical advocacy. They suggest, for instance, that there should be higher demands for more beds in university hospitals and better medications such as combined therapies that facilitate adherence to such complex treatment schemes. Paulo Teixeira, former director of the National AIDS Program, responded to the critique that NGOs’ dependence of public money might have captured the AIDS movement by arguing that they also have the right to use a fraction of public funds (Biehl 2007: 106). Nevertheless, collaboration between the NGOs and the Ministry of Health has provided fruitful results and is usually acknowledged as an important element of the successful Brazilian response to the AIDS epidemic (cf. Teixeira et al. 2004; Bastos et al. 2008; Nunn et al. 2009).

For the purpose of this thesis, this narrative evidences two important aspects. First, during this period the concern of AIDS advocacy was mainly with access to antiretroviral drugs, medical treatment of AIDS patients and a close collaboration with the National AIDS Program to design and implement the Brazilian response to the epidemic. There was no evidence that they were participating in the intellectual property debate and even less in the regulatory process of medicines, which was happening parallel to the AIDS campaign. When studying the AIDS treatment policy in Brazil, Nunn (2008: 85) found similar findings. Second, the relevance of the AIDS epidemic to the generic drug regulation was more nuanced. The costs of treating HIV/AIDS patients helped in placing access to medicines on the agenda of the Ministry of Health.



Until 1996, Brazil did not have patent protection, thus it was possible for local companies to produce one of the few drugs to treat AIDS patients at time, zidovudine (AZT). The production of antiretroviral drugs was the responsibility of private and public local pharmaceutical firms. For example, the local private pharmaceutical firm, Microbiologica, vertically produced the first batch of AZT in 1992, subsidised by the federal government. Microbiologica also produced two additional antiretroviral drugs, one of these nearly at the same time as the research-based firm launched its original version onto the market (Rabi 2007: 1422)<sup>42</sup>. This capacity to replicate medicines greatly reduced the costs of provision of AIDS treatment. However, the discovery of the triple therapy (or Highly Active Antiretroviral Therapy (HAART)) to treat AIDS patients in the mid-1990s (Ho 1995; Los Angeles Times 1996); the approval of the Intellectual Property Act in 1996 (Brasil 1996a); and a law mandating that the federal government should provide free and universal access to AIDS medicines in 1996 (Brasil 1996), represented additional challenges to the provision of antiretroviral drugs. This latter event refers to the bill sponsored by the former President and the President of the Senate, Jose Sarney. It received large support from Congressmen and did not place any restrictions on the amount of governmental spending (Nunn 2008: 87-91)<sup>43</sup>. The implications of these three events to the cost of AIDS treatment in Brazil is elaborated further in the next section.

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In short, by analysing these three streams with reference to the theoretical parameters presented in the second chapter of this thesis, it is possible to draw some conclusions. First, the diffusion of the WHO guidelines to implement generic drugs was important to inform and encourage decision makers in Brazil to regulate the off-patent medicines sector and introduce generic medicines. However, diffusion of generic drug regulation was not sufficient to initiate a reform in Brazil. The reasons for this,

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<sup>42</sup> Evidently, this governmental support and entrepreneurship to replicate innovative medicines increased the concern of multinational pharmaceutical firms with Brazil's absence of patent protection.

<sup>43</sup> Nunn (2008: 87-91) investigated the origins of Sarney's law and found little connection with AIDS activists. Anecdotal information suggests that Sarney had personal motivations for sponsoring this legislation (a family member living with HIV/AIDS) or even as a personal favour to the former director of the National AIDS Program, Lair Guerra (1985-1990 and 1992-1996).

as seen, relate to the domestic political institutions mediation, ranging from the content of the proposal to the local interests that successfully obstructed the bill in Congress and the Decree in the Judiciary. Second, patient advocacy groups were not proficient in regulatory policy language. They were unaware of the important reforms that were taking place in Brazil and that would have significant impact on their stances latter on.

A third conclusion from the antecedents of the generic drug reform refers to the lessons about the behaviour of participants of the policy process in Brazil. We cannot empirically observe that pharmaceutical firms' inner motivation in supporting or opposing the intellectual property legislation or generic drug regulation aimed at achieving an economic interest. This is particularly evident in the discussions of the intellectual property where it is possible to observe normative values in their discourse (e.g. the ethics of replicating medicines without permission of the inventor versus the effects of price monopoly on pharmaceutical assistance). Additionally, by observing the preference of AIDS activists, it is possible to evidence that they had framed their claims in human rights and were engaged in advancing one of the core values of the Unified Health System in Brazil, which is universal access to medical care. However, despite this apparently normative element of their preference function, it is also possible to observe, to some extent, economic stimulus in their actions. This is mostly evident as their collaboration with government evolved and most NGOs became financially dependent on the Ministry of Health and the World Bank loans. My intention here is not to deny the distinction between them. While firms are a group that indeed seek to produce and exploit profit, virtually all the NGOs working with AIDS patients are not-for-profit institutions. However, as demonstrated in this section, these are not their only goal and observing the content of their discourse offers a more diverse preference structure.

### **Reform period: political activism and uncertainty**

According to the critical juncture literature, major policy changes occur in a period of crisis (cf. Pierson 2004). There were three simultaneous contingent events in 1998

that disturbed the regulatory environment of the pharmaceutical sector in Brazil, creating a moment of uncertainty. Firstly, in March 1998 the price of some medicines increased by more than 200% (Folha de Sao Paulo 1998). Newspaper headlines expressed and reinforced the dissatisfaction of public opinion against the price of medicines: “Price of medicine increases above inflation rate”, “Brazil has the most expensive medicines in the world” and “The increasing price of medicines is offensive” (Folha de Sao Paulo 1998).

Secondly, an unexpected event turned particular attention to the pharmaceutical sector. On 19 June 1998, one of the most popular newspapers in Brazil reported that at least 14 women had become pregnant after using inactive birth control pills (Revista Veja 1998; Revista Veja 1998a). Microvlar, manufactured by the German pharmaceutical firm Schering-Plough, was at that time the third best-selling drug in Brazil (14 million units) and the top seller anti-contraception pill. While Schering argued that the inactive pills were a stolen trial batch, the media blamed the firm for its delay in reporting the case (Gaspari 1998). Additionally, two patients died after using fake cancer medicines. The outbreak of fake pills raised severe criticisms of the Ministry of Health and emotional negative publicity for pharmaceutical firms (O Globo 1998; Jornal do Brasil 1998a). Rough data estimates that, for each batch of 100 medicines, 20 were fake (Revista Veja 1998a).

The third event refers to the costs of AIDS medicine. With the introduction of universal access to AIDS medicines, the expenditure with antiretroviral drugs increased from US\$ 34 million to US\$ 336 million dollars from 1996 to 1999 (Nunn et al. 2007 - with the Ministry of Health data). This reflects both the increased number of patients receiving treatment (from 35.900 to 73.000) and the necessity of newer and patent-protected drugs to treat them (*ibid*). Implementation of universal access to AIDS treatment would require not just an effective logistic distribution and laboratory infrastructure, but also financial resources (Nunn 2008). While the former would be covered by the World Bank loan, the latter would be the sole responsibility of the Brazilian government. To graft the attention of the public opinion to relevance of this issue, and to hold the Minister of Health accountable to the legislation

mandating universal access to AIDS medicines, the director of National AIDS Program (at that time National Coordination of HIV/AIDS), Pedro Chequer (1996-2000 and 2004-2006), began using the media to pressure:

Like AIDS activists in the early 1990s, one of Chequer's political tactics was to use the media to hold Congress and the Health Ministry accountable for its new legal commitments to financing drugs for all PLWHA under Sarney's Law. He used media to publicly lobby the health minister and Congress for increased funds for public treatment and care, requesting increased spending for AIDS care. [...] One strategy [...] was to publicly announce low ARV drug stock before it depleted, which was most common for expensive protease inhibitors. Chequer immediately engaged the media and NGOs, announcing that he was waiting on an official government response (Nunn 2008: 98).

This triple distress occurred in the pharmaceutical sector when President Fernando Henrique Cardoso (FHC) decided to bring the Economist Jose Serra, former Senator and Minister of Planning, Budget and Management (1995-1996), to the Ministry of Health. An experienced politician and presidential hopeful, Serra's approach to the problem was aggressive. First, he determined intervention for five days of Schering's manufacture unit; second, he personally visited many of the affected women, committing to provide them with health assistance (see figure 3); third, he determined the creation of regional prosecutors to investigate crimes in the pharmaceutical sector and drafted a proposal to create a Health Surveillance Agency; and fourth, he edited a Ministerial Directive (Portaria 802/1998) to regulate the distribution of medicines and established quality control mechanisms (O Globo 1998; Gazeta Mercantil 1998a; Jornal do Brasil 1998b). Media attention to the price of medicines, the costs of AIDS treatment, and fake pill outbreaks contributed to the agenda setting. Jose Serra positioned the pharmaceutical sector as a flagship, championing many important regulatory reforms. For clarity, I have divided the Generic Drug reform into two periods: first, the legislative discussions and, second, the resolutions and policy instruments to implement it.

Figure 3. Newspaper images of Microvlar incident



Source: Jornal do Brasil (1998b). Note: “Drugs: Minister visits woman that a took inactive pill”



Source: Gaspari (1998). Note: “Schering can turn into flour”.

## **Reform phase 1: Parliamentary negotiations and the Generic Drug Act**

Although Serra had a lot of experience in politics and public management, he knew less about the health sector. Facing the crisis in pharmaceuticals, he focused on interventions to lower the price of medicines and enhance quality control, by suggestions of the Federal Deputy Ronaldo Cesar Coelho:

There is no reference to generic medicines in my inauguration speech. To be honest, I did not know very well about this. Who brought me this issue for the first time was Ronaldo Cesar Coelho. [...] He was PSDB's federal deputy and brought me the idea [the bill of Eduardo Jorge on Generic Medicines]. So, Ronaldo [...] linked me to the issue [...] and I then became interested in this matter (Serra 2009).

The first step to implementing a generic drug policy was taken through a ministerial directive that established Brazil's first National Drug Policy in October 1998 (Ministerio da Saude 1998). Although pharmaceutical assistance is cited in the complementary law that regulates the health care system in Brazil (Law 8080/1990), until that moment there was no formal resolution within the Ministry of Health to organise a medicines policy. Among others, the National Drug Policy introduced the guidelines for rational use of medicines and a generic medicine programme. As mentioned by Serra, he was advised by the Federal Deputy, Ronaldo Cesar Coelho, to advocate for a law to regulate the generic drug market in Brazil. He requested a governmental official, Gonzalo Vecina Neto, to revise all the bills that dealt with generic medicine regulation (in addition to the Bill 2022/91, there were two other proposals enclosed to it)<sup>44</sup> and other international guidelines on this issue (Vecina-Neto 2009). Additionally, Serra travelled to Europe, the United States, India and Israel to better understand the context of pharmaceutical regulation (Serra 2002; Serra 2009). Despite the extensive field research for this project, there was hardly any evidence of pharmaceutical firms or any interest group pressured to implement

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<sup>44</sup> During field research for this project, I contacted the two former deputies that presented these bills. Victor Faccione informed me that he was no longer involved in politics and could not remember his intention in supporting this project or the debates around this topic. Alberto Goldman, who is currently heading the government of Sao Paulo state with Jose Serra, informed that this project unfolded from discussions in the Congress Commission of Intellectual Property. However, it was also argued that introduction of several similar bills or amendments to a bill are strategic use of the Congress norms to block or delay its approval.

the Generic Drug Act; the deliberations on Parliament to approve this bill and the discussions in the National Health Surveillance Agency further exemplify this.

As opposed to the negotiation to vote for the patent system, when there was a clear division in Congress lobbying between local and foreign interests, during the Generic Drug legislation debate this polarisation was less evident (cf. *Jornal do Brasil* 1998). Pharmaceutical firms' demands were Abifarma's responsibility, which had both national and multinational members. It was not possible to assess precisely why Abifarma became responsible for representing the pharmaceutical sector and advocating in this matter. Although national and multinational firms opposed to the use of INN, there was no consensus among them on the bioequivalence affair. During data collection for this project, no official statement of Alanac or Interfarma regarding the generic drug reform was found. However, interviews with government officials and local entrepreneurs suggest that local firms were radically opposed to the introduction of bioequivalence requirements. An influent founder of a Brazilian pharmaceutical firm, when questioned about the position of local firms, commented:

We thought this would be insane [bioequivalence tests]. Brazil did not have the structure to do something like this. This is so true, that the first generic drugs were developed outside the country or as part of doctoral thesis in USP [a prominent university in Sao Paulo] because no one here knew how to do this. Nobody knew how to do it! (Interview with local pharmaceutical businessman A 2009)

By contrast, multinational firms and Abifarma were openly supporting bioequivalence requirements right after the enactment of the patent legislation in 1997 (Abifarma 1997b). However, it is vital to reinstate here that I could not find any evidence that Jose Serra included bioequivalence into his proposal because of Abifarma's pressure. In fact, as we shall see later on in this chapter, the relation between these two was highly conflictive during this period. Abifarma sponsored a Seminar on 22 October 1997, a year before Serra became Minister of Health, to discuss the challenges and opportunities of the pharmaceutical sector in Brazil. It brought together ministries, pharmaceutical sector representatives, politicians and government officials. Among the different topics related to economic and industrial incentives, it also discussed the introduction of generic drugs (Abifarma 1997b):

The pharmaceutical industry is open to discuss, with the parliament or executive government, a generic drug policy to Brazil. [...] It would be sad if we introduce a generic drug policy to the poorest and ended up creating more problems to their health; because it is not income class A and B that will use it. [...] Build an excellent generic drug policy in Brazil as long as respects health surveillance parameters adopted in the United States and Europe, which is bioequivalence and bioavailability. There, if generic drugs do not provide these requirements simple it will not launch the market (Jose Eduardo Bandeira de Mello was executive president of Abifarma - Mello 1997).

Note that the argument of the bioequivalence requirement was linked to a discourse of quality control. Generic products would be legitimate because they equalled medicines produced by Merck Sharp Dohme, Glaxo, Pfizer and other well-known firms. In other words, medicines that are an equal copy of their patent version would be more credible/safe than those that are not. Note how the content of multinational pharmaceutical firms' demands differs from the period of 1993, when Brazil first attempted to regulate these products. After the introduction of the Patent Act, innovator companies knew that at some point they would face a generic drug competition. Whether they wanted to or not, they would have to live with this unpleasant substitution of their products. They could pay some lip service to it or resist by boycotting any attempt to encourage generic drug substitution (with a high probability of bringing negative media coverage to their business). Thus, an adjustment in their preference with respect to generic drug regulation was necessary, as opposing to generic drug competition and regulation was less possible. Consequently, they proposed a regulation that, at least, could reduce (to some extent) the competition in this sector. My intention is not to dismiss the relevance of the bioequivalence test as an important step in the pharmaceutical manufacturing process, but it is to call attention to the political element of this regulatory concept (cf. Carpenter and Tobbell 2011). This certainly reduces the number of firms qualified to produce generic medicines, but also has a clever frame of legitimising the quality of the product which, once diffused, could be difficult to reverse. On the other hand, local pharmaceutical manufacturers were less supportive of the off-patent market regulation.

A former governmental official, who participated in the negotiation process of the Generic Drug Bill, commented that both national and multinational firms were opposed to the generic drug regulation to some extent. The multinational



pharmaceutical firms were concerned with the trademark and prescription rules. The government's proposal required that all similar and innovator drugs should display the INN in labels, while the trademark would present a size no more than 20% of the generic name (Interview with government official A 2009). Note that, although this is an apparently meaningless aspect of regulatory policy, it matters a great deal to this sector as marketing strategies represent an important element of the product cycle (cf. Comanor 1986). Pharmaceutical firms promote their trademarks heavily among doctors and pharmacists and reducing or excluding their brand names would require a paramount effort from their business. After negotiations, it was agreed that, in the label of innovator products, the trademark would be displayed in a higher font size and the BNN or INN would come right below, with a reduction of 50% compared to the brand name. On the other hand, all products registered as generic drug could only be commercialised by its BNN or INN.

Furthermore, multinationals also demanded that generic drug substitution should only be allowed under a doctor's written request. However, the government did not agree to negotiate this aspect of the bill; thus, if doctors did not agree with generic substitution, they should write on the prescription "substitution not-allowed" (Interview with government official A 2009). This information is confirmed by a letter from Abifarma to the Ministry of Health in 1998, requesting that the new legislation: a) should not allow generic substitution in drug retail stores given that the retailer is not technically prepared to replace medical prescriptions; b) called attention to the fact that the bill did not request the presence of pharmacists in drug retail stores; and c) did not agree with the mandatory prescription by the generic drug name in contracted institutions of the Unified Health System. It suggested that this would harm brand-name manufacturers and, in particularly, local firms, given that their products were not protected by patent, were also brand named and would be substituted by a generic drug (Felippe and Mello 1998).

By contrast to the negotiation with multinational pharmaceutical firms, the governmental official described the debate with national industries even harder: "The discussion with national industry regarding registration was more complex. The local

pharmaceutical industry was afraid of disappearing if they had to face a legislation mandating bioequivalence. They knew bioequivalence would be expensive” (Interview with government official A 2009; Vecina-Neto 2009). In 1998, the cost of producing a bioequivalence test was around US\$100.000 per product (Interview with local pharmaceutical industry informant A 2009). Assuming that a local firm had 20 products in its portfolio that must comply with this rule, the total cost to adjust the whole portfolio would be two million dollars. If the product failed in the first test, a new test would be required, increasing the costs even further. Although Brazil has a long tradition of local (private and public) production of medicines, these firms were medium-sized, family-owned and with limited latitude for risky adjustments. Consequently, the fear for local entrepreneurs was that the remarkably high costs involved in complying with this new regulatory regime would force them to exit the market (Interview with government official A 2009; Interview with local pharmaceutical businessman B 2009; Interview with local pharmaceutical industry informant A 2009). The founder of a local private pharmaceutical company commented on this period of uncertainty:

[...] You introduce new elements to the regulatory regime in operation in Brazil until then. What happened was that Brazilian firms, facing a new situation and very diverse compared to the one in operation before... got scared because the issues involved [...] It is natural that there was some frightening given the volume of changes that happened at the same time. Evidently, this produced a discomfort (Interview with local pharmaceutical businessman B 2009).

Interviews and documents consulted suggested that the Minister of Health put enormous effort into convincing Congressmen to introduce the generic drug legislation (Coelho in Camara dos Deputados 1998: 26010; Interview with government official A 2009). One of the governmental officials interviewed commented that Serra went personally to the Congress several times to pressure Congressmen to approve the Generic Drug Bill (Interview with government official A 2009). The sponsor of the generic drug bill, Federal Deputy Eduardo Jorge (left-wing PT), was in political opposition to the Executive Government (centre-right PSDB), which could have been problematic given that Serra and Ronaldo Cesar Coelho’s proposal were significantly stricter than the ones proposed in the original bill of 1991. Eduardo Jorge commented on this during the Chamber of Deputies floor

discussion: “What we are voting on here is an agreement. I am dropping my original proposition [...] that is, generic medicines commercialized only by its generic name [...]”. He then justifies his decision: “If I keep my initial proposition, somehow I would play the game of those who do not want a generic drug policy; I would forever delay its introduction” (Jorge in Camara dos Deputados 1998: 26000). The bill was approved unanimously by all party leaders in the Chamber of Deputies on 19 November 1998.

Records of the floor discussions highlight the relevance of Deputy Ronaldo Cesar Coelho and the Minister Jose Serra in championing the agreement (Camara dos Deputados 1998). A push for counterfactual analysis shows that, had the original project been accepted, regulation of off-patent medicines would have little adjustment in terms of technical requirements. Simply using the generic name (INN) in labelling would transfer the marketing strategies to the industry name, i.e. publicity strategies would focus on the firm’s name and in the credibility of the producer. Competition would remain at the final stage of product development but with little adjustment in terms of industrial plants or manufacturing practices, placing the pharmaceutical sector in Brazil on a different path than the one that has been chosen. Thus, the Generic Drug Act introduced a new product into the market, forcing a rearrangement of the pharmaceutical sector. Previously, competition was among two pharmaceutical products: an innovator (or reference) product versus a similar drug. After the 1999 Generic Drug Act, competition turned to three pharmaceutical products: an innovator (or reference) product, a generic drug (interchangeable with its reference product) and a similar drug (not-interchangeable with a reference product). Note that this disturbance in the pharmaceutical sector is not just because of the content of the reform but is also due to the Ministry of Health signalling a strong credible commitment to implement all the aspects of this regulation. To do so, the Minister of Health expanded the crisis in a different way, as we shall see later on in this chapter.

Similarly to other studies of pharmaceutical sector reform in Brazil, this thesis also acknowledges the leadership of the Minister of Health in championing the

introduction of generic drugs in Brazil (Franca 2004; Dias and Romano-Lieber 2006). However, this thesis suggests a more nuanced analysis by demonstrating that his entrepreneurship was only possible given the crisis that preconditioned the Generic Drug Act. Had Serra been a Health Minister in early 1990s it is very unlikely that this reform would have been possible. As the previous section has demonstrated, the sequence of three events (Congressional effort to pass bill on generic drugs, the enactment of the IP law and AIDS epidemic) paved the way for the generic drug reform in 1999. Limiting the analysis of Generic Drug reform to vote-seeking or political leadership misses these important aspects of the regulatory process. As suggested in chapter 2, by narrowing the analysis to periods of institutional reform it is likely that the role of particular actors will be emphasised (cf. Pierson 2004: 141). However, these studies ignore the conditions that facilitated, limited or channelled entrepreneurship activity.

It is important to recall here the absence of HIV/AIDS activists in contributing to the discussions of the regulatory process, as their agenda focused on access to HIV/AIDS treatment (Galvao et al. 2011). However, the relevance of the AIDS epidemic was to the agenda-setting stage rather than in collaborating in the debates about the content of the reform. If Brazil had not enacted a Federal legislation mandating universal access to antiretroviral drugs, and the National AIDS Program had not voiced the rising costs of these medicines, there is a chance that the crisis in the pharmaceutical sector would be less visible. Furthermore, while the AIDS epidemic was crucial to the agenda-setting process, interest group activity was less. There is hardly any evidence to show that pharmaceutical firms' activity influenced the agenda of reform. Despite the previous movement of Abifarma to debate generic medicines and the bioequivalence concept in 1997 (Abifarma 1997b), it is not possible to credit them for the outcome of the Generic Drug Act. When balancing the forces pro-reform, the World Health Organization and interests groups seem to have less influence on the policy outcome than the Executive government activism. Finally, had Brazil not implemented an intellectual property law in 1996 it would be less likely that the government would include the bioequivalence concept into the regulatory rules. To be considered a bioequivalent product, the generic drug

necessarily needs to be compared with an innovator/patented medicine. Thus, this exercise of counterfactual analysis highlights the relevance of these events to the decision taken in 1999.

### **Reform phase 2: Governmental activism to implement generic drugs**

The Generic Drug Act was approved in February 1999. Simultaneously to the generic medicines debate, Serra decided to reform the sanitary surveillance secretariat, which was ripe with corruption, and to create an independent regulatory agency, the Agencia Nacional de Vigilancia Sanitaria (ANVISA) (Piovesan 2002; Piovesan and Labra 2007; Mello et al. 2008). The recently established National Health Surveillance and the Ministry of Health were responsible for establishing the regulatory parameters for implementing the Generic Drug Act. But how to make the generic drugs happen? In other words, how could they induce pharmaceutical firms and drug retailers to supply generic drugs? How would they encourage health professionals and consumers to request generic drug substitution? The discussion in Congress was the first part of the reform, whilst establishing the resolutions to regulate the market was the second part of the story and perhaps the most controversial. This section describes governmental activism in the three years that followed the bill approval and is divided between political actions taken by the Ministry of Health and the decisions taken by the National Health Surveillance Agency (ANVISA) to regulate the market. Note these events happened simultaneously and are divided here for clarity. This is particularly important as it builds up the evidence that pharmaceutical regulatory processes are not always an input of interest group activity and that government activism can indeed reformulate the preferences and demands of the pharmaceutical sector.

#### Ministry of Health political pressure

The Minister of Health, Jose Serra, was personally engaged in helping to bring about the Generic Drug Act. This section describes three political strategies that caused to destabilise potential opposition forces to the reform: (A) tensions with the pharmaceutical association Abifarma, (B) incentive to create a business association pro-generic drug, (C) negotiation with multinational pharmaceutical firms over the

price of antiretroviral drugs. Needless to say, these decisions were taken simultaneously and are divided here for heuristic purposes:

#### (A) Tension between Serra and Abifarma

In the first semester of 1999, right after the approval of the Generic Drug Act, two unexpected events affected the atmosphere of the pharmaceutical sector. Firstly, changes in the economic policy. The Minister of Finance and the President of the Central Bank decided to adopt a monetary policy based on a free floating currency and inflation target, which was previously under the control of the Central Bank. Devaluation of Real (Brazilian currency) brought about a significant impact on the annual business plan of multinational subsidiaries in Brazil. According to an informant that had close connections to a pharmaceutical association at that moment, the currency devaluation would reduce firms' budgets by nearly 30% for that year, deeply jeopardising multinational annual business plans (Valor Economico 2000; Interview with pharmaceutical industry association informant A 2009). Because of this unexpected economic crisis, multinational pharmaceutical firms decided to adopt strategies to delay the entry of generic drugs for a few months to recover their losses (these are discussed below) (Interview with a pharmaceutical association informant A 2009). A second unexpected event was the fact that a segment of the local pharmaceutical sector was engaged in unfair competition, advertising similar drugs as if they were a generic drug product. These products were not registered with the ANVISA as a generic drug, thus could not be advertised as such. Figure 4 and 5 show an example of an unauthorised 'generic drug' advertised in 1999. The first legitimate generic drug entered the Brazilian market only in 2001 (Pro-Genericos 2009a).

Figure 4. Illegitimate advertisements of generic medicines in July 1999

**Este é um legítimo genérico do Teuto**

**Hidroclorotiazida**  
**Diurix®**

50 mg

**PRINCÍPIO ATIVO**

VENDA SOB PRESCRIÇÃO MÉDICA

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**MARCA DE QUALIDADE E EFICÁCIA**

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Source: Revista ABCFarma (1999)

Figure 5. Illegitimate advertisements of generic medicines in July 1999

**GENÉRICOS NEO QUÍMICA**

Preferência nacional

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This was a moment of great tension between the pharmaceutical sector and the Ministry of Health and perhaps the peak of the crisis in the pharmaceutical sector. While Abifarma demanded a prompt governmental response to stop the advertisements of the unlicensed pharmaceutical products, the association also began its own public campaign to inform consumers about generic drugs. On the other hand, governmental officials accused Abifarma of boycotting generic drugs, delaying the entry of these products and generating confusion around the issue. During field research for this study, controversial versions were reported about this episode. This study did not attempt to explain or investigate this disagreement. However, the tension between pharmaceutical companies and Serra's administration is important in understanding how this reform evolved.

Apparently, because the government was slow to respond to its demands, Abifarma used the media to inform the population and used the judiciary to block the advertisements of the unlicensed generic drugs. There was an aggressive mass media campaign to make the population aware of the new legislation. Several informative notes were published in popular magazines, newspapers and advertised on TV shows (cf. Abifarma 1999). According to its promoters, it intended to educate the population about the different pharmaceutical products and suggested that the quality of the 'false-generic drugs' would be lower than their respective brand names. Government officials condemned this strategy, arguing that Abifarma was sowing doubt on the credibility of generic drugs among consumers, and delaying and avoiding the introduction of these products. Simultaneous with the media campaigns, Abifarma filed several complains at the Public Ministry (body of autonomous magistrates composed of public prosecutors) arguing that a segment of local firms were commercialising pharmaceutical products unlicensed by ANVISA (Ministerio Publico do Estado do Rio de Janeiro 1999; 1999a; 1999b). These two strategies had a profound negative impact on Abifarma's image. Government and public opinion understood this as an attempt to boycott generic drugs. In an interview for this study, both sides commented on this episode:

Multinational industry did not support generic medicine. But they could not assume this in public. [...] their campaign said national product was crap. Basically, they spent 7 million reais in 15 days, in all magazines, newspapers saying “National product is crap”. “Be careful with national product”. That didn’t help me, although Gabriel [representative of Abifarma] swears to God that his intention was to help me, to help ANVISA (Interview with government official A 2009).

I can guarantee to you, I give you my word. Abifarma was informing the population that generic drugs did not exist at that time and when it had arrived we would communicate it to the population. [...] We paid a higher price for that. [...] I have in my CV this position that seemed that I was against generic medicines. I still keep everything proving exactly the opposite (Interview with pharmaceutical industry association informant B 2009).

There was no generics and they advertised that there was [mentioning a group of national pharmaceutical industries]. [...] We did a campaign on TV, radio, with doctors clarifying what was a generic drug. [...] We went to court to denounce this but the fight was political not judicial. Judicial decisions take 2 or 3 years. So what happened was that we were marked by society as against generics, against reducing the price of medicines, supporters of multinationals. Terrible from a political perspective (Interview with pharmaceutical industry association informant C 2009)

The government informant suggested that there was a campaign from firms to block or delay the introduction of generic drugs, while representatives from this sector denied this suspicion, arguing it was an attempt to inform the population about different pharmaceutical products available in the Brazilian market. This study did not attempt to investigate or clarify the different sides of this debate; the relevance is that these episodes fostered the crisis in this sector and the opportunity for the Minister of Health to push his agenda further on. To destabilise collective action and possibly opposing forces, Serra took two decisions. First, he refused to receive the executive president of Abifarma, Jose Eduardo Bandeira de Mello. All consultations with the sector were taken with firms individually, breaking down collective action (Valor Economico 2000). In an interview with a popular newspaper, Serra mentioned that “The Minister and the Ministry will not receive the president of Abifarma because he only creates misunderstandings” (Folha de Sao Paulo 2000). Second, Serra requested Congress to investigate the cost structure of the pharmaceutical sector through a Parliamentary Investigative Commission (PIC) (Serra 2009). In a year of sub-national elections, Federal Deputies welcomed Serra’s demand, particularly to investigate such a controversial sector of the economy. The fanfare surrounding the PIC received extensive media coverage, promoting a negative image of the pharmaceutical sector and reducing their leverage. It could also be argued that, by proposing an extensive investigation into the pharmaceutical sector, Serra fostered

the crisis in order to implement his ambitious agenda. During the investigation into pharmaceutical firms' cost structure, it was announced to Congressmen that multinational firms were trying to block the implementation of generic medicines, turning their attention to the problem and further expanding media coverage (Agencia de Noticias da Camara dos Deputados 2000). Despite the many accusations raised in this period, none of them was confirmed after the criminal investigation (Ministerio Publico do Estado de Sao Paulo 2003). Nevertheless, all these episodes were important to give credibility to the Minister of Health, destabilise the pharmaceutical sector collective action and increase press coverage on this matter. Thus, with the sector disorganised and weakened, the government could proceed with its regulatory agenda.

#### (B) Creation of policy advocacy pro-generic drug

A decisive step, and perhaps strong evidence to show how the Brazilian government influenced pharmaceutical politics, is the creation of the Brazilian Association of Pharmaceutical Industry (Pro-Genericos). Pro-Genericos was established in 2001 to aggregate the interests of generic drug manufacturers. Surprisingly, the initiative of consolidating the lobbying group was a suggestion of the Minister of Health, Jose Serra (Sindicato da Industria de Produtos Farmaceuticos no Estado de Sao Paulo 2006; Interview with local pharmaceutical industry informant A 2009). Jose Serra commented in an interview for this study: "I induced [generic manufactures] to create a national association of generic manufactures. I saw there was one in the United States and I thought: 'Brazil must have one, to defend the interests of this sector'. And that coincides with public interest" (Serra 2009). A representative of pharmaceutical industries confirmed:

The proposal [to create Pro-Generios] was given by Minister Jose Serra in a meeting with generic drug manufactures. I was there. As soon as he gave the idea, I replied: 'Let's create it within the syndicate'. All other representatives agreed at the same time. There was no reason to articulate separate [separate from the syndicate]. Our effort was to aggregate all of them: generic manufacturers; medium prescription and Over the Counter; national and foreigners; large and small (Interview with local pharmaceutical businessman B 2009).

Pro-Genericos was located within the Sao Paulo Syndicate of Pharmaceutical Industries (Sindusfarma). Its role in defending the sector's demand was enhanced

when the former director of the Division of Generic Drugs/ANVISA, Vera Valente, joined the association in 2003. Valente began an aggressive advocacy to publicise the generic drugs. For example, it was during her tenure that Pro-Genericos first advocated against patent extension. Additionally, given the negative image associated with Abifarma during the Parliamentary Inquiry Commission and regulatory process of generic medicines, its members decided to reorganise interest representation, creating a new Federation to represent their preferences and demands. This will be further elaborated in the next chapter; for now, however, it evidences how the pharmaceutical sector was slowly accommodating to fit the government's agenda.

### (C) Tension between the Minister of Health and multinational firms

Parallel to the discussions on Generic Drug Act, Serra advocated further important reforms in the pharmaceutical sector. These were the adjustments in the intellectual property law, to scale up the production of antiretroviral drugs in public pharmaceutical industries, and international advocacy of pro-essential medicines. Although these reforms were not directly related to generic drugs, they had implications on the pharmaceutical sector and to the path of generic drug regulation in the 2000s, thus it justifies exploring them in this chapter.

First, Jose Serra advocated heavily for reforms in the patent system in Brazil. One adjustment refers to the flexibility in overriding patent protection (i.e. issue a compulsory licence) (law 10196/2001 amended article 71 of the patent law). Another refers to a reformulation in the process to register pharmaceutical patents, mandating that the National Patent Office (INPI) and the Health Surveillance Agency (ANVISA) should both revise these requirements (this is known as prior approval consent). Finally, the third reformulation in the patent system refers to an authorisation to allow pharmaceutical firms to begin researching the manufacturing process of a generic medicine prior to patent expiration and prepare for market entry at the moment of patent expiration (i.e. early working provision) (article 43 of the IP law, VII). The existence of the local production of medicines (public and private) evidently gave Serra credibility to champion the reforms (cf. Nunn 2008 - chapter 5;

Shadlen 2009). The study of Shadlen suggested some level of support of local producers to these reforms in the patent system (Shadlen 2009); however, during field research for this study it was not possible to trace any sort of lobbying activity either pressuring or proposing Serra to push these reforms. Apparently, these were political decisions, taken within the executive/legislative government, to restructure the stringent patent system approved in 1996 and to facilitate the process of price negotiation of antiretroviral medicines with multinational pharmaceutical firms.

Second, the studies of Nunn (2008) and Nunn, Fonseca *et al.* (2007) provide extensive analysis of the decision of Jose Serra to scale up production of antiretroviral drugs in public pharmaceutical industries. The authors argue that local production would not just help overcome the rising costs of ARV but would also be an instrument to negotiate prices with multinational companies. The flexibilities in the IP law aforementioned would facilitate this negotiation. If Brazil's public industries had the capacity to replicate patented antiretroviral drugs, Serra could consider issuing a compulsory license either to produce these drugs or to threaten to issue a compulsory license to bargain prices with multinational firms (Nunn 2008: 112). Brazil is world-renowned for this innovative strategy of negotiating prices of antiretroviral medicines (cf. Ford et al. 2007; Nunn et al. 2007). As we shall see in chapter 6, medicines produced in these public pharmaceutical firms are not generic drugs as they are not interchangeable to an innovator product. Nevertheless, what it is important to understand now is that this decision also fostered the crisis in the pharmaceutical sector and added to the negative image of the sector, increasing the legitimacy of the Minister of Health to move forward his ambitious agenda.

Thirdly, the decision to adjust the IP legislation and price negotiation with multinational pharmaceutical firms led to an intense international debate between Brazil and the United States at the World Trade Organization (Sell 2002; Odell and Sell 2003; Sell and Prakash 2004). After this, Serra's advocacy on pharmaceutical regulation went cross-borders. In May 2001, Jose Serra gave an enthusiastic speech at the opening session of the 54th World Health Assembly of the United Nations:

There is an urgent and imperative need for debate on the importance of increasing the supply of generic medicines and of accelerating their entry into national markets. [...] The policy of encouraging production of generic medicines will continue [...]. Thanks to these policies as well as to the national production of not-patented AIDS drugs we were able to reduce the purchase prices of these medicines by seventy per cent. (Serra 2001: 2).

Brazil's international advocacy activities are widely known and have been the object of many studies (c.f. Odell and Sell 2003; Biehl 2004; Sell and Prakash 2004; Nunn 2008 - chapter 6; Nunn et al. 2009a). For instance, Brazil sponsored several resolutions at the United Nations agencies (redefining the issue of access to medicines as a human right); headed a coalition that led to the Doha agreement *TRIPS and Public Health*, making it easier for developing countries to use TRIPS safeguards; and promoted the introduction of AIDS medicines into the WHO Essential Medicines List (cf. Sell and Prakash 2004; Nunn et al. 2009a). This international activism highlights the commitment of the Brazilian government to the domestic reforms, but it was also during this process that Brazilian AIDS activists began their participation in pharmaceutical regulatory processes (elaborated in chapter 6). Similar to the other political decision mentioned above, there is hardly any evidence that Serra was pressured by patient advocacy groups or local pharmaceutical firms to put forward this international agenda. In a period when the international community was discussing compensatory interventions to the economic globalization (e.g. Seattle and Bangkok contestation), Serra was viewed as a "Social Minister". He was ranked in 2000 as the most competent Minister of Cardoso's administration according to an internal evaluation (Gazeta Mercantil 2000a). For his remarkable activism, Serra was quoted by the Newsweek Magazine as a "Guerrilla Minister", who "went after pharmaceutical companies, slashing "abusive prices" for brand-name drugs and flooding the market with cheap generics"(Newsweek 2001).

In conclusion, all these simultaneous controversial political decisions built up to destabilise the collective action in the pharmaceutical sector, creating a period of deep uncertainty and forcing pharmaceutical firms to redefine their preferences and strategies to fit the governmental regulatory agenda. Additionally, the governmental mobilisation had a strong social appeal, convincing public opinion to back these decisions and increasing its legitimacy. Nevertheless, the Health Surveillance Agency also had the crucial role of designing the resolutions to regulate the generic

drug sector and to implement it. This chapter now turns to analyse this step of the regulatory process.

#### National Health Surveillance: regulatory resolutions and enforcement

The responsibility to formulate the resolutions to regulate the generic drug sector was on the recently created Health Surveillance Agency (ANVISA). After approving the legislation in Congress, it was necessary to have a regulatory framework, defining the parameters to commercialise the generic drugs in Brazil. However, as a recently established institution, ANVISA did not have technical expertise to formulate these regulatory guidelines (Vecina-Neto interview in Dias and Romano-Lieber 2006 p29). Serra allocated a member of staff from the Ministry of Health, Vera Valente, in ANVISA to put the law into effect. A Division for Generic Medicines was created apart from other pharmaceutical regulatory departments with a direct connection to the president of the ANVISA to facilitate the formulation of these rules (Interview with local pharmaceutical industry informant A 2009). As director of the Generic Medicines Division (*Gerencia Geral de Medicamentos Genericos*), Vera Valente was responsible for personally overseeing market development and defining the regulatory framework for registration, testing and marketing of generic drugs.

It is crucial to highlight the context of uncertainty and the lack of expertise of Brazilian officials in dealing with the new regulatory framework. Because Brazil did not have specialised centres or experts to produce bioequivalence tests, it was necessary to build up a technical capacity to implement them. The former president of ANVISA, Gonzalo Vecina Neto, commented on his limited knowledge on bioequivalence/bioavailability tests:

We had to learn. It was very difficult to learn. There were a lot of things we didn't know, a lot of things people said were done and nobody did it, or lots of things people said, nobody did it and everybody did it. There are still questions nowadays. But, at that time, we were in the dark [...] we were lost. Until then, bioequivalence was done outside Brazil, but how would it be the national [...]? (Vecina-Neto in Dias 2003: 39)

Given the lack of expertise in this sector, a consultant from the University of Texas, Salomon Stavchansky, was hired to develop the technical parameters for generic

drug registration. According to Vecina-Neto, this was an important step in designing the Brazilian framework. However, he suggests that the final resolution became similar to the American one, which he now understands as too stringent (Vecina-Neto in Dias 2003: 39). The first resolution to regulate the generic drugs was published in August 1999 (Resolucao 391/99, ANVISA 1999). Vecina-Neto speculated that, had Brazil not taken Salomon's advice to implement a regulatory framework analogous to the United States, the norm might not have been so stringent (Vecina-Neto in Dias 2003: 40). The former president of ANVISA attributes this result to the constraints imposed by the political momentum (the presidential election and the crisis in the sector) as this required a prompt and strong governmental response, leaving less time to reflect about other possibilities (*ibid*). Note that policy emulation did happen, as the new version of the Generic Drug Bill was not a creation of Brazilian government. However, the learning process was not a sufficient condition to initiate a reform (also evidenced by the failure to implement the WHO recommendation in 1993, otherwise a likely moment for introduction of these products in Brazil).

After this, ANVISA's regulatory framework for generic drugs was reformulated four times between 1999 and 2002 to incorporate/adapt to reactions of the pharmaceutical sector, but also because of problems identified during public consultations (Dias and Romano-Lieber 2006). The study of Dias (2003) provides a comprehensive description of these normative directives issued by ANVISA during this period. The author suggests that the government could not wait for the market's self-regulation or to be captured by interests against generic drug. Thus, ANVISA monitored market reactions, enforcing new resolutions when needed. The author concludes that the control was so stringent that there was no way of escaping the generic drug path (Dias 2003: 51). Essentially, ANVISA's policy instruments to regulate the market can be divided into supply and demand mechanisms.

(A) Induce generic drug demand. A key pillar to introducing generic medicines in Brazil was to mobilise public opinion and increase the demand for generics. Because mass media campaigns would require large amounts of resources, the Minister of



Health opted for an alternative strategy to keep the generic drug issue in the media (Dias and Romano-Lieber 2006). He travelled around different regions in Brazil to publicise generic drugs, while government officials attended medical conferences and consumer group meetings to spread the relevance of these products. Regardless of the effort to stimulate a generic drug demand, these products were still not appearing in retail drug stores. A newspaper article published in October 1999 highlighted the delay in commercialising generic drugs: “[...] governmental attitude seems to be demoralized. The question is, ‘are generic drugs going to happen now?’ The constant postponing of deadlines indicates a discredit in public authorities and generates even more questions about this reform” (Folha de Sao Paulo 1999b). Newspaper articles speculated that the lack of generic medicine supply was due to: 1) generic medicines were still under analyses by ANVISA, which would require at least six months for the first product to be launched; 2) retail stores were embargoing these products; 3) generic manufacturers did not have the scale to cover the high demand for generic drugs (Folha de Sao Paulo 1999a; Folha de Sao Paulo 1999d; Estado de Sao Paulo 2001). To neutralise the possible objection of retail stores and stimulate the supply of medicines, the government introduced several normative directives to induce the supply.

(B) Induce generic drug supply. A first strategy was to pass a resolution mandating that all drug retailers must display a list of generic medicines registered with ANVISA [Resolucao 45/00 and Resolucao 99/00] (ANVISA 2000; ANVISA 2000a). Consumer Groups monitored and provided a list of retailers that did not sell generic drugs, aiming to penalise those who were unresponsive (Jornal de Brasilia 2000a; Jornal de Brasilia 2000b). Another resolution mandated generic manufacturers to disclose their sales balances monthly [Resolucao 78 August 21<sup>st</sup> 2000] (ANVISA 2000b). They were to include total drug production, manufacturing capacity, total number of products sold, to whom they were sold and information about market size and participation. These reports suggested that there was a problem of scale, i.e. firms were not able to produce and cover the increasing demand for generic drugs (Dias and Romano-Lieber 2006).

In response to the lack of scale, ANVISA took two controversial decisions: it adopted a fast-track procedure to accelerate drug approval<sup>45</sup> [Decree 3675 November 28th 2000] (Brasil 2000), and stimulated multinational generic manufacturers to invest in Brazil by importing drugs or through joint ventures with national industries. The Agency also recognised bioequivalence tests conducted in United States, Canada and Europe, accepting products approved in these countries to accelerate the introduction of generic drugs [Decree 3841 June 12th 2001] (Brasil 2001). Although the fast-track method had benefited national industries as much as multinational generic manufacturers, local producers promptly reacted to the privileges offered to the international manufacturers. It is suggested that the government's intention was to introduce generic drugs into the market rather than to only protect local companies. Jose Serra commented on this mechanism:

[...] And I went to the United States and England, to see how generic works there. [...] And in Israel, I went there because of Teva and I wanted to attract Teva to Brazil. It was to break this invisible market barrier, the problem [...] they were not producing. The principal president of Teva told me they had also bought raw materials from India. And I went to India to stimulate Indian laboratories to produce in Brazil. I was there, I saw the laboratories. We were successful in some things. It is not a matter that Brazil did not have the capacity to produce generics, but it was necessary to enter the market, and stimulate the others (Serra 2009).

(3) Additional regulatory instruments. Additionally, ANVISA created a new visual identity to generic medicine labels (which should show a yellow stripe and the letter G) to facilitate identification of generic medicines, thus making it easier for consumers to differentiate between the pharmaceutical products available in Brazil (innovator, generic and similar drugs) (see figure 6).

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<sup>45</sup> Fast-track process would allow then a grace period of 1 year to provide bioequivalence tests.

**Figure 6. Generic drug label according to Brazilian regulatory rules**



Source: adapted from ANVISA (2010).

All these resolutions signalled to the pharmaceutical sector that the government was alert and ready to make adjustments and commitments to fully implement the Generic Drug Act, despite the initial bottlenecks. The lack of expertise of the newly created ANVISA required a lot of learning and exchange of information about how to best regulate these products. This process involved a strong bargain with pharmaceutical industries, drug retailers and health professionals, but also the Regulatory Agency counted on the expertise of an American consultant.

## Conclusion

This chapter adds to the analysis of generic drug regulation in Brazil in several ways. It has demonstrated that there are records of the diffusion of the WHO and the United States normative guidelines. Brazil did not formulate a new paradigm in the regulation of generic drug products. However, the diffusion of these norms was not sufficient to initiate Brazil's reform. Similarly, there is hardly any evidence of interest group activity in pressuring the reform or supporting government intervention in their trademarks and manufacturing process; this contradicts explanatory perspectives that suggest the regulatory process was captured by firms with an economic stake in the regulatory activity (cf. Stigler 1971).

The findings of this chapter suggest that generic drug reform was "politically driven" but also resulted from a conjuncture of institutional development. Unlike previous studies that had credited the Minister of Health as a key condition to the reform, this

chapter suggested a more subtle analysis. It acknowledges his role in championing the regulatory process, but this was only possible thanks to the opportunity created by the crisis in the pharmaceutical sector (with the price of medicines and the media complaints about the fake drugs), the particular time in the electoral cycle and the creation of ANVISA. Furthermore, the three antecedent events that occurred in the 1990s have also channelled the reform by different means.

The Brazilian government had tried to implement generic drugs before, following the WHO recommendations but, as is seen in this chapter, the institutional context was not favourable. Even if Serra had been the Health Minister in 1993, it would be very unlikely that this reform would have been possible. Nevertheless, previous generic drug bills greatly legitimated and facilitated the decision taken in 1999. The intellectual property law enacted in 1996 made the regulation of the off-patent medicine imperative. How and when this would happen was less evident. Finally, the sequence of the AIDS epidemic, the institutional constraint to provide universal access to antiretroviral medicines, the diffusion of a new therapeutic consensus to treat this disease led to an increase in the number of patients. Thus, the cost of treatment was seen as a threat to the sustainability of the National AIDS Program and expanded and highlighted the agenda of pharmaceutical regulation. All these events together, happening in a particular moment in time, influenced the enactment of the Generic Drug Act in Brazil and influenced its content. A narrow analysis of the reform period (1999-2002) would rule out this important contextual information, putting more emphasis on the individual entrepreneurship and missing out the important conditions of his entrepreneur activity.

Exploring these historical circumstances is also important when understanding the content of interest group demands and the extent to which they have influenced the policy change. The description of the political demands of pharmaceutical firms suggests that local producers were concerned with the magnitude of the pharmaceutical reforms taking place in the 1990s. In particular, this group was apprehensive about the generic drug regulation as this would require costly investments to exclude trademarks, to restructure their manufacturing plants and

processes to fit the bioequivalence norm. Thus, they were less sympathetic with the idea of having the government interfering in their business. In contrast, multinational pharmaceutical firms reaped many market advantages during this period with the enactment of the intellectual property and the stringent design of the generic drug regulation. Although this group was similarly concerned with the government interfering in their trademarks, the risk of this reform to their business was significantly lower vis-à-vis local pharmaceutical producers (public and private). Finally, this chapter has also demonstrated that the AIDS epidemic and its patient advocacy had a relevance to the reform by giving visibility to the crisis in the pharmaceutical sector, although their demands focused squarely on provision of treatment.

The period of uncertainty and institutional instability was important element that made possible the reform, against the resistance of these groups. During the discussions and design of the generic drug regulation, the minister of health, Jose Serra, took several simultaneous decisions (e.g. suggested a Parliamentary Investigative Commission to the pharmaceutical sector) that fostered the crisis in this sector, deepened the uncertainty and created an opportunity to move forward his ambitious and unattractive agenda. The analysis of the generic drug reform in Brazil resembles the theoretical propositions suggested in Chapter 2. During periods of crisis actor's preferences become unstable and with the outcome uncertain, it is difficult for them to make rational decisions. Thus, this would lead them to rethink their preferences and demands and perhaps adapt to the governmental agenda. Unfortunately, the enactment of the Generic Drug Act and the enforcement of ANVISA was no guarantee that the legislation would stick. To understand its development it is also necessary to look at the political effects of this rule in the behaviour of participants in pharmaceutical sector in Brazil. The following chapters deal with the aftermath of the generic drug regulation, as the theoretical chapter discussed, only by looking at how actors behaved in the subsequent period it is possible to say if there was or not a crucial change in actor's behaviour, in turn how did this happen helps in understanding policy development.

## **5. Assessing the generic drug regulatory process in the 2000s: governmental intervention, market demand and local pharmaceutical industries**

Chapters five and six assess the development of the generic drug policy. While the previous chapter assesses a period of significant disruption and uncertainty in the pharmaceutical sector in Brazil, these two chapters assess a moment of institutional stability compared to its antecedent. We know from the literature review that generic drug regulation persisted even after Serra left the government, but we know less about how this happened. In what ways have the generic drug regulation influenced the governance of the pharmaceutical sector in Brazil? The theoretical approach for this thesis has suggested that the policy process can influence the behaviour of stakeholders as they interpret the new institutional context and re-evaluate their preferences and demands. Consequently, the analysis starts by looking at the institutional context in the 2000s and the three actors in the generic drug regulation, that is, the government, market demand and suppliers of generic drugs. The introductory chapter of this thesis has mentioned the relevance of these three actors to the policy development and, for this reason, they served as a guide to assess this stage of the policy process. However, this regulation has also generated unexpected effects on other stakeholders in this sector, such as public pharmaceutical factories and patient advocacy groups, which were clustered for heuristic purposes and is the object of the analysis of chapter six.

This chapter is organised into three parts and the conclusion. The first part presents the economic outcomes of this regulatory policy, reviewing the vitality of these products in the pharmaceutical sector in Brazil. However, economic analysis alone is ill-equipped to understand how this policy evolved the way it did. The second part of this chapter assesses how government advocacy for generic drugs evolved after the Cardoso and Serra administration. The second part also discusses the market demands for generic drugs. Both were mentioned in the introductory chapter of this

thesis as core elements to the development of a generic drug policy (cf. World Health Organization 2001). Because assessing market demand is a relatively difficult concept to operationalise (public opinion polls would be a better way to do it), this thesis relied on academic studies, business reports and others as a proxy to understand how health professionals and the population perceived these products. As the analysis suggests, both elements are unable to explain the development of generic drug regulation in Brazil. Governments have been less politically active on this matter and there is controversial and conflicting information about how health professionals and the population received these products. Thus, the third part of this chapter discusses the role of suppliers. The literature review and the economic background information suggest that private local pharmaceutical producers have been leading the rank of the generic drug sector. Also, studies suggest a remarkable competitive and industrial development of these firms after the Generic Drug Act (Abreu 2004; Quental et al. 2008). However, we know even less about how this happened. Particularly puzzling is that, as demonstrated in the previous chapter, local pharmaceutical producers repealed this government intervention in their business. This chapter concludes by summarising the aggregated effect of the new institutional context on these three actors (government, market demand and supply), how it empowered local pharmaceutical producers, and reflects on the structure of the interest group in this sector in Brazil.

### **Background: economic outcomes**

The generic drug reform had an extraordinary impact on the pharmaceutical sector market. Using business analysis and academic studies, this section discusses the economic performance of generic drugs, highlighting the vitality of this sector in Brazil. According to the Brazilian Association of Generic Drug Manufacturers (Pro-Genericos (2009), the market share of generic drugs is increasing steadily and represented 14% of sales in 2008. Registration of generic medicines at the National Health Surveillance Agency (ANVISA) increased from 893 in 2002 to 3000 in 2006 (Pro-Genericos 2009), which implies that more products have been entering the market. The demand for generic drugs has also been progressing since 2001. The

market share for generic drugs (in volume) was ~17% in 2008, an increase of 359.7% since 2003 (see also annex 4 for further market evolution data) suggesting this is a promising segment of the pharmaceutical sector in Brazil (Pro-Genericos 2009).

Looking at the retail market, where expenditure is mainly out-of-pocket, studies suggest that the generic drug market is segmented according to income, therapeutic class and geographical area. The studies of Frenkel (2008; 2008a), Valentim (2003) and Bertoldi, Barros *et al.* (2005) infer that the main beneficiaries of generic drugs are income class B and C in Brazil. Different income segments have different elasticity to price variation. While income class A are willing to pay the costs of sophisticated or brand name drugs, class B and C are more sensitive to price variation. For Class D and E, the authors suggest that generic drugs competition has little impact on access to treatment as this segment relies on medicines provided by governmental programmes. This projection was corroborated by a public opinion survey conducted in 2006 in eight Brazilian capitals involving 800 people, which demonstrated that, among generic drug consumers, 30% are class A/B. The middle class represented 36% of consumers and class D/E 34% (Gazeta Mercantil 2006; Guia da Farmacia 2006)<sup>46</sup>.

In terms of the therapeutic class, the best-selling generic drugs are antibiotics and medicines to treat chronic illness (Montrucchio *et al.* 2003; Vieira and Zucchi 2006; Rosenberg *et al.* 2008; IMS 2009; Pro-Genericos 2009; Rosenberg 2009). For instance, the price of two drugs to treat diabetes (*metformina*) and hypertension (*atenolol*) decreased by 64% between 2004 and 2007 (Pro-Genericos 2008). Vieira and Zucchi (2006) compared the prices of generic and original drugs in Brazil between 2000 and 2004. The authors found that generic drugs entered the market with an average price of 40% lower than their patented version and this difference tended to increase over the years. Other studies suggested similar findings (Sutton

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<sup>46</sup> I could not have full access to this study as this was conducted by a consultancy agency ([www.marketanalysis.com.br](http://www.marketanalysis.com.br)). Nevertheless, I thank the director of this agency, Fabian Echegaray, who kindly provided me with a briefing of this research. Further information was also found in press releases.



2004; Monteiro et al. 2005; Miranda et al. 2009). However, because of market competition and retailing commercial strategies, there is a considerable price variation among generic drugs. For example, a study of the Consumer Protection Foundation/Sao Paulo in January 2010 has shown a difference of 1.415% in the price of Hidantal® and its generic version Fenytoine (neuractive drug) (G1 2010; O Globo 2010; Secretaria de Justica e Defesa da Cidadania and Fundacao de Protecao e Defesa do Consumidor 2010).

Nevertheless, generic drug competition did not reduce the price of patent medicines and consumers loyal to patent drugs might face an increase in the cost of their treatment, as suggested by the studies of Vieira and Zucchi (2006) and Fiuza and Lisboa (2001). For example, the average price of Elli Lilly's Keflex®, a best-selling antibacterial, increased from ~ R\$15.00 in 2000 to R\$ ~30.00 in 2008 (Rosenberg 2009). Consequently, the population would have an additional incentive to shift to a generic drug. However, unlike these authors, the study of Nishijima (2008) using a different methodology found that patent drug prices decreased after generic entry and also that these prices were sensitive to the number of generic drugs on the market.

The prescription of generic medicines is still low but is increasing over time, representing 20.9% of the total in 2006, compared to 11.8% in 2002 (Pro-Genericos 2008). However, for particular substances, generic medicines have achieved high prescription levels, for example omeprazole (88%), cephalexin (77%) and fluconazole (65%) (Espicom Business Intelligence 2007; Pro-Genericos 2009 - with Close UP MAT and Inestra/IBOPE data). According to estimates of the Brazilian Association of Generic Manufacturers, generic drug competition has saved consumers nearly US\$ 5 billion in out of pocket drug expenditure since 2000 (Pro-Genericos 2009). Particularly important would be an assessment into the effects of generic drugs on health outcomes or access to medicines. However, so far it has not been possible to identify any study that has considered this issue. Some analysts use market information as a proxy for access to medicines. To sum up, all this information tells us is that the generic drug market is evolving in Brazil with an apparent re-structuring of the pharmaceutical sector. However, only a qualitative and

in-depth assessment of the regulatory process of generic drugs in this period can provide information on how and why this happened.

### **Government advocacy and market demand**

This section assesses the participation of government in the development of generic drug regulation and also analyses the health professionals and population demands and perception of these products.

### **Governmental intervention**

As discussed in the previous chapter, the generic drug reform was conditioned by a political decision and an intense governmental advocacy occurring in a particular period of the electoral section and triggered by a crisis in the pharmaceutical sector. During the presidential election campaigns in 2002 and 2010, the mayor elections in 2004 and gubernatorial elections of 2006, Jose Serra largely used the implementation of generic medicines as one of his foremost achievements (PSDB 2002) (see figure 7). It is not possible to say precisely whether his inner motivation to introduce generic medicines was political or vote-seeking, as this is not available for empirical observation. In fact, Serra's own interpretation to the decisions taken during his administration, and particularly to respond the AIDS epidemic, was discussed in a working paper presented at Princeton University in 2004 (Serra 2004). Citing Hirschman's concept of latitude in performance of decision makers, Serra justified that the health sector, and especially the HIV/AIDS epidemic, allowed no room for manoeuvre, or delays and errors that were less acceptable compared to those in other areas (*ibid*: 16). Thus, the decision-maker was constrained to act, given that the consequences of inaction would be severely judged by public opinion and with far-reaching consequences to the health sector in general.

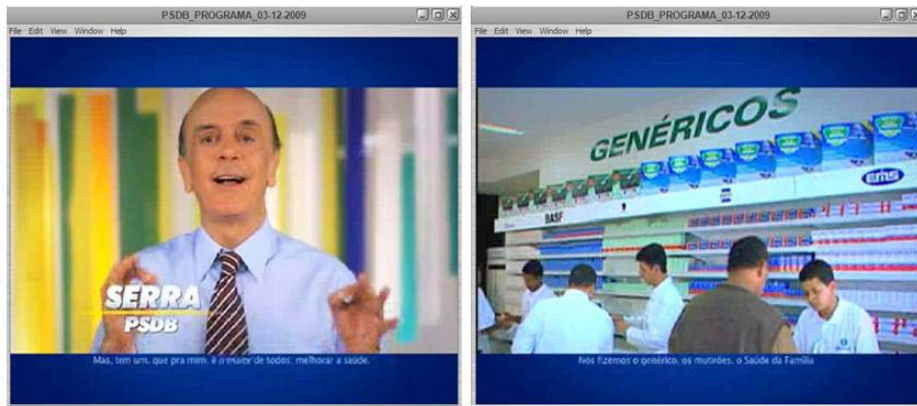
Nevertheless, the use of this policy in Serra's political campaigns is evident and he is keen on recalling attention to this matter. He has claimed that, although generic drugs are not an invention of his administration, it was thanks to his political activity that these pharmaceutical products were introduced in Brazil. It fostered market

competition and lowered the price of medicines, particularly those treating chronic diseases. One of his campaign promises was to further expand this initiative (Folha de Sao Paulo 2010a). To say that Serra took political advantage of this reform is not to condemn him; politicians are accountable to voters, and reaping credit for their decisions is a fundamental aspect of the political realm. Regardless of this credit-claiming activity, Jose Serra lost the presidential elections of 2002, which brought a left-wing government into power for the first time in more than 40 years. In 2004, he was elected mayor of the city of Sao Paulo and, in 2006, governor of Sao Paulo state but lost the presidential election in 2010. Thus, he is distant from pharmaceutical policymaking decisions in Brazil and less able to continue influencing the path of generic drug policy.

Figure 7. Jose Serra's Presidential election campaign, 2002 and 2010



“Generic [drugs] are celebrating 10 years”



## Governo do PSDB revolucionou a saúde



A saúde foi uma das áreas que mais recebeu atenção no governo do PSDB. A população foi beneficiada por vários programas com reconhecimento internacional e o ministro José Serra foi considerado o melhor ministro da Saúde do mundo.

Com Fernando Henrique, o Sistema Único de Saúde (SUS) melhorou, ao contrário do que aconteceu depois que Lula assumiu. Basta perguntar aos pacientes.



O QUE O PSDB FEZ E O QUE O PT DEIXOU DE FAZER | A VERDADE DOS NÚMEROS | 15

Source: [www.psdb.org.br](http://www.psdb.org.br) (2010).

How did the government advocacy for the generic drugs evolve after Serra's administration? By comparing the policy initiatives taken by the current government with the ones during Serra's administration, it is clear the governmental political activity in generic drug advocacy has reduced considerably. Several evidences suggest that there was a reduction in mass media campaigns to inform and stimulate a demand for generic medicines. For instance, in 2003, the Senate Sub-commission on Health requested a Public Consultation to investigate how to improve the legislation on generic medicines (Consultoria Legislativa do Senado Federal 2003; Estado de Sao Paulo 2003). Senator Papaleo Paes, in his plenary speech, pointed out that one of the findings of this consultation was that the government discontinued initiatives to stimulate generic drug demand (such as mass media campaigns):

We are not facing an issue that can be treated as an ideological bias or political party stamp. This is a policy [generic drugs] to the Brazilian population, focused above all on poor citizens. [...] It can be observed that Federal Government discontinued a policy adopted by previous administration. Current administration withdrew, for example, activities to make the population aware – essential to make the population aware of the relevance of generic drugs [...]. It is essential to reactivate public utility campaigns, adequately informing consumers, blocking irresponsible drug store salesmen that act as if they were doctors. [...] It urges that Federal Government demonstrate efforts to consolidate our generic drug market in order to increase consumers' achievements (Paes 2003).

During field research for this project it was not possible to identify any newspaper or policy statement produced by the successor administration on generic drugs. In a newspaper article, a government official for the National Health Surveillance Agency commented on the government orientation regarding generic medicines: “The Minister Humberto Costa [2003-2005] reduced the status of this Division [generic drug] at ANVISA. There was no reason to emphasise generics when this was the political agenda of another President candidate” (Estado de Sao Paulo 2003). Interviewees were asked to comment on the government's activity to inform the population about generic drugs. A number of interviewees commented that the government decided to suppress the generic drug campaign because it was strongly connected with the previous Health Minister:

The first Minister of Health in Lula's government [Humberto Costa], he used to say openly within the Ministry [...] I know someone who was in a meeting with him, and it was forbidden to talk about generics. It was forbidden to say positive things about generics, it was forbidden to talk about generics. It is unfortunate, but there was sustainability already (Interview with local pharmaceutical industry informant A 2009).

Generics were Serra's stamp. From the point of view of awareness campaign, induction, PT [the incumbent political party – Workers Party] has done basically nothing. Talking about generics is talking about Serra. This became a stamp. Therefore, from an institutional perspective, governmental perspective, it is evident that nothing will be done to clarify the population about generic medicine, to substitute a product X by a generic [...]. I think this was a big mistake, in the sense that transforms generics into a political discussion rather than a public health discussion (Interview with local pharmaceutical businessman B 2009).

An analysis of the organisational structure of ANVISA reinforces these statements. The agency directive N° 593/2000 established a General-Management of Generic Medicines (GMGM) at the same level as the General-Management of Medicines (GMM). Both managers were classified as chief-manager and receiving the same salary range, being level 2 (*Cargo de Gerência Executiva II*) (ANVISA 2000c). As discussed in the previous chapter, the GMGM was responsible for coordinating the

generic drug regulation; its status of General-Management department not only suggested this policy was a priority, but also gave direct contact to ANVISA's president. However, a rearrangement of departments took place in June 2003, immediately after the new government came to power. The agency directive N°385 downgraded the GMGM and its manager salary range was reduced to level 3 (*Cargo de Gerência Executiva III*) (ANVISA 2003b). Finally, a further rearrangement in 2009 dissolved the GMGM and divided its functions into two lower-level departments: Coordination of Generic and Similar Drugs Registration (CRMED) and Coordination of pos-Registration (COPRE) (ANVISA 2009). It was not possible to assess exactly why ANVISA decided to rearrange the structure of medicine's regulatory department, but it clearly split the responsibility of the GMGM and reduced the priority of generic drug regulation vis-à-vis other pharmaceutical products and the bargaining power within the Agency. This is not to say that Brazil had reduced its regulatory standards to register generic drugs, but it evidences that there is no priority among pharmaceutical products.

Despite these observations that claim that the current government would try to eclipse the previous administration's generic drug policy, it might also be possible that the current administration has a different understanding of how to tackle the problems with access to medicines. Clearly, Jose Serra's approach to increasing access to medicines was to stimulate competition in the pharmaceutical market, lower the price of medicines and thus increase access. In this sense, the Director of the Department of Pharmaceutical Assistance/MoH, Norberto Rech, explained in an interview to a newspaper in 2003: "Generics indeed play an important role, but the government has responsibility to conduct broad public policies rather than policies to a specific sector. There is an intention to increase use of generics, but public policy cannot be market's policy" (Estado de Sao Paulo 2003). The Minister of Health, Agenor Alvares (2006-2007), reaffirmed this position: "We believe that publicity on generic drugs must be the responsibility of laboratories. It would be an incoherence if the government promoted advertising for a fraction of the pharmaceutical sector" (Valor Economico 2006a). Finally, a governmental official further elaborated these perspectives when interviewed for this study:

Many times generic manufacturers came to the Ministry of Health for what? To request campaigns to induce generic use. This is not the role of the State. These campaigns must be done by producers. This is a market issue. If we had few generic medicines, maybe this would be reasonable. The Ministry of Health has made efforts with the creation of the National Committee to Promote Rational Use of Medicines. And within rational use of medicines policy and promotion, generics have a relevant spot (Interview with government official B 2009).

This information was corroborated with policy statements. Indeed, in March 2007 the Ministry of Health created the National Committee for the Rational Use of Medicines. However, according to the meeting reports, little has been discussed about generic drugs (Ministerio da Saude 2010a). Its focus has been at best on disseminating general guidelines on rational use of medicines to mass public and health professionals. Furthermore, the current administration introduced for the first time in Brazil mechanisms of co-payment, which is under the responsibility of the Brazilian Popular Pharmacy Program (the government-managed programme was created in 2004, while its private sector-managed programme was established in 2006)<sup>47</sup> suggesting a new orientation to the pharmaceutical assistance programmes.

In this sense, the Ministry of Health has also shifted attention from generic drugs to another controversial initiative, which is the Health Industry Complex project. President Lula's administration has focused strongly on developing an industrial policy for the pharmaceutical sector (elaborated further in the following section that deals with local producers). In March 2007, when Jose Gomes Temporao was appointed to the Ministry of Health; this initiative became also a focus of health policy. Temporao is a physician and an academic of the National School of Public Health, with extensive experience in health management and policy. His research team has been engaged in studies of technological innovation in the health sector backed by Marxist and neo-Schumpeterian theories (cf. Gadelha et al. 2003; Temporao et al. 2003; Guimaraes 2004; Temporao et al. 2005; Gadelha 2006; Casas 2008)<sup>48</sup>. Temporao developed an ambitious project, *Mais Saude* (More Health), to

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<sup>47</sup> The former is state-owned drug stores and uses mainly public produced drugs (similar drugs); the latter is private-owned drug stores that provide mainly private produced drugs (both similar and generic drugs). Tables x and x1 show the evolution of these programmes.

<sup>48</sup> The Marxist perspective discusses the infiltration of the capitalist production process into the health sector and its structural determinants on health practice (e.g. the inter-relation of pharmaceutical

reduce external dependency of strategic health and technological sectors (Ministerio da Saude 2010a). It is supported by the argument that there is an increasing deficit in the trade balance of health supplies, reaching US\$ 6.75 billion in 2008 (the pharmaceutical sector alone represented a deficit of US\$ 3.3 billion in the same year) (Moyses-Junior 2005). According to government officials, this scenario places Brazil's health system in a dependent and vulnerable situation (Moyses-Junior 2005; Guimaraes 2009). One of *Mais Saude* objectives is to stimulate the local production of medical devices, medicines and other strategic health supplies through mechanisms such as government purchase power or public and private partnership.

All the evidence presented so far suggests that there was a reduction of governmental dissemination and promotion of generic drug products. The reasons for this might be associated with a strategy to reduce the political leverage of generic drugs, or even a reorientation of the Ministry of Health pharmaceutical policies. On the other hand, the Health Surveillance Agency has expanded its capacity to regulate these products substantively. For example, as seen in the previous chapter, when Brazil decided to introduce bioequivalence requirements to its regulatory norm there were no experts or centres to conduct these studies and many had to be conducted abroad. While in 1999 nearly 80% of bioequivalence tests processed in ANVISA were conducted abroad, in 2008 nearly 70% of these had already been prepared by local centres (Cristofolletti 2008). Today, there are 51 centres certificated to conduct bioequivalence studies, of which 23 are international and 28 national institutions (*ibid*). ANVISA has also constantly revised and expanded the BE guidelines (see, for example, resolutions 103, 134, 895 and 899 in 2003 and 34 issued in 2008). The design of these technical parameters for generic drug regulation in Brazil has been based on extensive cooperation with pharmaceutical firms (cf. ANVISA 2003b; ANVISA 2004a).

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industries within the capitalist production system and the consequences of medicines as a trade commodity). The neo-Schumpeterian approach discusses the configuration of production based on technological innovation. The health sector can be a producer of economic development simultaneously connected to its sanitary role. If so, this group of researchers and now policy-makers understand that the management of the health sector must take into account both its sanitary role and its capital accumulation face. It places technological and industrial development within public health policies by integrating production of service and industrial goods to social interests (economic growth, innovation and welfare enhancement) (Casas 2008).



To sum up, the introductory chapter of this thesis has suggested that government advocacy is important to stimulate a market demand for generic drugs, thus it is a crucial element of this policy. However, as seen so far, Serra's succeeding administration has demonstrated less interest in fostering market competition in the pharmaceutical sector through the promotion of generic drugs. The evidence presented here also suggests that the government discourse has changed, incorporating preferences of rational use of medicines as a core agenda in pharmaceutical assistance, but also a concern with decreasing the external dependency on foreign capital in this sector. Thus, policy content also shifted to instruments that focus on research and development of active pharmaceutical ingredients (raw materials) and medicines. Nevertheless, enforcement of bioequivalence tests and the other requirements to register generic drugs is afoot and the norms have been designed in collaboration with pharmaceutical firms.

### **Market demand**

The development of the generic drug market could also be explained by the support of consumers, who demand these pharmaceutical products, thus contributing to policy sustainability. Collecting primary data on the effects of generic drug policy on consumers and health professionals is not the objective of this study. However, market demand is a core element by which to assess the development of generic drug regulation and cannot be ignored. Thus, this study relied on secondary data (dilemmas and methodological choices were already discussed in chapter 3).

Despite the increasing growth of the generic drug market in Brazil, there is still low consumer awareness of generic drug products and slow acceptance by physicians (Valente 2006). Studies suggest that there is confusion on how to differentiate the pharmaceutical products (innovator, similar and generic) and a lack of confidence about the quality of generic medicines (Bertoldi et al. 2005; Folha de Pernambuco 2007; Tribuna do Norte 2007). For example, a study conducted in 2002 using household samples found that, although 86% of the population interviewed understood that generic drugs cost less, 56% failed to differentiate between generics

and other medicines. Results were worse among people with low schooling and economic status. There are many brand-name drugs on the market (similar drugs) that cost less than generics, which can “indicate a possible misunderstanding between what consumers think and what they are actually using” (Bertoldi et al. 2005: 1813). Similar findings were reported by Carvalho and Raffin (2006) in a study of social representation of generic drugs conducted between 2002 and 2003 with drug retail consumers. The authors suggested that users usually refer to generic drugs as lower-priced medicines that serve an immediate demand and have questionable quality (*ibid*).

In terms of generic drug prescription, academic studies, market assessments and a number of newspaper articles point out that health professionals are still resisting prescribed generic drugs (Valente 2006; Espicom Business Intelligence 2007; RNCOS E-Services Private 2007; Pro-Genericos 2009; Rosenberg 2009; Folha de São Paulo 2010). For example, a survey conducted in 2006 in eight Brazilian capitals assessed the opinion of 55 health professionals. While 44% of the health professionals believed that generic drugs were not as reliable as original drugs, among those who trusted generic drugs, 17% did not prescribe them (Gazeta Mercantil 2006). In a public hearing in the Federal Senate in 2009, the representative of ANVISA, Tatiana Lowande, questioned the inaction of health professionals in prescribing generic drugs. She suggested that doctors should inform the Agency about drugs they believed were not safe and urged that the general public and the Federal Police should monitor this behaviour (Camara dos Deputados 2009; Federação Nacional dos Farmacêuticos 2009; O Globo 2009a).

As suggested in the first section of this chapter, market intelligence data points out that diabetic patients were the largest beneficiaries of generic drug competition. However, in an interview for a newspaper in 2003, the physician and president of the National Association of Diabetic Assistance, Dr Fablo Fraige Filho, reported that he prescribed a generic version of a drug to treat hypertensive diabetic patients and it did not work: “I won’t prescribe it ever again” he declared (Isto e 2003). During field research for this project, interviews were conducted with diabetic associations and

government officials responsible for implementing public policy for diabetes and heart diseases to assess their position on generic drug policy. Similar to what has been described so far, there was little consensus on the safety of generic drugs. One interviewee suggested that generic drugs are approved by the regulatory agency through the influence of politicians and raised doubts over the manufacturing conditions of local pharmaceutical firms (Interview with Diabetes patients informant A 2009). The intention here is not to investigate whether these assertions are reliable or not; but the fact that a high level representative of diabetic patients, an opinion leader, raised concerns about these pharmaceutical products reinforces the argument that there is still a fragile confidence on generic drugs. Both representatives of diabetics patients interviewed agreed that it seems that people who can afford them prefer the original products rather than the generic version (Interview with Diabetes patients informant A 2009; Interview with Diabetes patients informant B 2009).

Looking at institutional purchasers, such as the public health system, the demand for generic drugs is also problematic. Public pharmaceutical assistance programmes would represent an important demand for generic medicines. The Generic Drug Act (Law 9787/1999) mandates that all public purchases and prescription of medicines should be done by the generic name. However, recent studies that assessed the availability of medicines in Brazil has demonstrated that, in the public sector, generic medicines are less available than similar drugs (Miranda et al. 2009; Pinto et al. 2010). For most medicines (71.4%), the availability of bioequivalent generic drugs was less than 10% (Miranda et al. 2009). The authors suggest that public purchase of medicines has greatly privileged similar drug medicines. If so, what these numbers indicate is that there is an inconsistency between what medicines physicians prescribe in the Unified Health System (SUS) and what medicines are provided by public health facilities.

Why does this happen? The legislation that regulates public procurement of medicines (and other goods and service contracts) determines that, if all technical requirements are met, the provider that offers the lowest price wins (reverse bid) (Law 8666/1993). By contrast, the generic drug legislation determines that in this

case generic drugs should be given the priority (Law 9787/1999). Miranda *et al.* (2009) speculate that this might be happening because: (a) generic drug producers are not interested in participating in public procurement, (b) better prices offered by similar producers, or (c) perhaps difficulties in following the legislation requirements. The Director of the Department of Pharmaceutical Assistance/Ministry of Health, Jose Miguel, when interviewed for this thesis declared that, although similar and generic drugs do not have the same technical parameters, usually similar producers offer a lower price, which leaves the government officials with no other option than to buy the similar drug (Miguel 2009). He reports that, if priority is given to a generic drug producer that offers a higher price, then Public Accountings or Courts could interfere in the operation, causing delays in the supply of medicines. He also pondered that this could be a problem in designing public procurement, but so far there was no attempt to reformulate or debate this.

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In summary, this section has demonstrated that the political engagement and commitment of the Ministry of Health in promoting a generic drug competition in Brazil has reduced considerably. On the other hand, the health professionals and the population demand and acceptance of these products is still fragile. The documents and papers reviewed suggest a conflicting perception as to whether they see these products as unsafe, or even a misunderstanding regarding the different pharmaceutical products available within the Brazilian market. While government and demand support are important elements of a generic drug regulation, so is the supply of these products. Thus, the next section discusses the local pharmaceutical firms' stances.

### **Local pharmaceutical manufacturers**

Local pharmaceutical producers were the least likely group to adapt to the reform. Their fear was that remarkably high costs to adjust to this new regulatory regime would force them to exit the market (Valente 2009; Vecina-Neto 2009; Visconde-Jr

2009). For example, the small pharmaceutical industry Sebadel founded in 1953 had a revenue of US\$ 1 million per year. Half of its 200 products were required to provide bioequivalence tests, costing US\$ 100,000 per product. This is nearly the entire industry's annual revenue (Rumos 1999). The generic drug regulation established not just a stringent framework but also a short period for producers to adjust to the new rule. Responding to the complaints of the local pharmaceutical industries about the costs of bioequivalence tests, the former Minister of Health, Jose Serra, commented in a newspaper interview in 1999, "those who cannot afford this test cannot produce generics. More important than anything is the population's health" (Serra in Rumos 1999: 31). As the government made credible commitments to the reform, the fate of similar drug producers would then be either to adjust and convert to a generic drug (interchangeable with its innovator version) or provide evidence of incremental innovation and request a new patent at the National Patent Office (INPI).

Surprisingly, local firms not only managed to adapt to the regulatory reform but also became market champions in the pharmaceutical sector (see figure 8 for the generic drug market and table 9 for the pharmaceutical sector as a whole). For those who managed to adapt, generic drugs became a big business opportunity. Brazilian pharmaceutical industries account for 88% of the domestic generic drugs market. Generic manufacturers estimate an investment of US\$ 350 million by 2012 (G1 2007; Estado de Sao Paulo 2007a - with IMS Health data). In 1999, the local pharmaceutical firm EMS was 29<sup>th</sup> in the ranking of pharmaceutical industries in Brazil, and in less than 10 years it became the market leader in the generic drug sector. Similarly, Eurofarma, Biosintetica and Medley – all family-owned – had an impressive market performance over the same period. The director of the Brazilian Association of Pharmaceutical Industries (Alanac), Sara Kanter, declared in a newspaper article: "the commercial battle is in progress. If similar industries do not adapt quickly, it is expected that they will lose all the conquered space to generics and innovator medicines" (Kanter in Rumos 1999: 28).

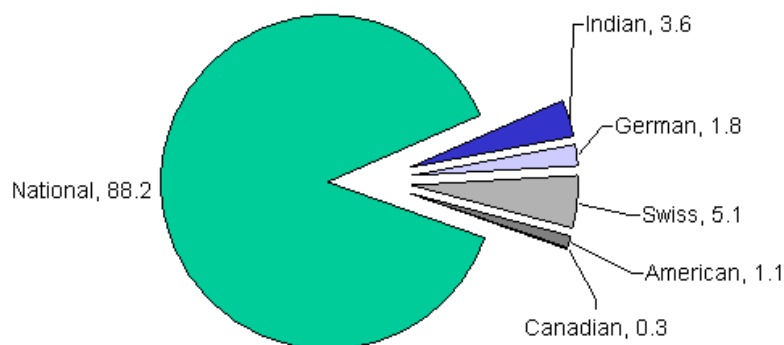
**Table 9. Ranking of pharma. industries in Brazil (US\$), 1999 and 2005-2009**

Industry	1999	2005	2006	2007	2008	2009	% participation
EMS	29	5	3	2	1	1	6,59
Sanofi-Aventis	1	1	1	2	2	2	6,24
Ache	3	2	2	3	3	3	5,68
Medley	32	7	6	4	4	4	5,67
Novartis	2	4	4	5	5	5	4,1
Eurofarma	28	9	8	6	6	6	3,90
Pfizer	7	3	5	6	7	7	3,06
Bayer Schering	23	6	7	7	8	8	2,86
Astra Zeneca	19	22	20	15	12	9	2,37
Boehringer	11	8	9	9	9	10	2,24

Source: (Pro-Genericos 2009 - with IMS Health data)

Note: Names/numbers in blue refer to Brazilian industries.

**Figure 8. Market share (vol) of generic pharma. producers in Brazil in 2007**



Source: (Pro-Genericos 2008 - with IMS Health data)

However, the cost to adapt was high. Local industries that, until then, were based on a marketing and distribution business had to reformulate their industrial plants, create their own laboratories to provide pharmacokinetic tests and contract tests in humans (some bioequivalence tests require clinical trials). It was estimated that the infrastructure cost around U\$ 1 million for each firm; added to that, expenditure in testing each product was between U\$ 200 and 250 million per product (Exame 2005a). For instance, Eurofarma, one of the largest local industries, from 2000 to 2005 invested nearly U\$ 45 million in pharmacokinetic tests (Exame 2005a). How and why did local pharmaceutical firms become highly supportive of generic drug policies and become market leaders in the pharmaceutical sector? To assess these questions, this section looks at local producers' preferences and demands after the reform in different events (note that this division is for analytical purpose): 1)

reorganising collective action: creation of Pro-Genericos, Febrapharma and extinction of Abifarma; 2) adjusting similar drugs: ANVISA's resolution 133 and 134/2003; 3) framing generic drugs: the industrial development and the access to affordable, safe and efficient medicines campaign; 4) using comparative advantage: Brazil's pharmaceutical businessmen.

### **Reorganising collective action to accommodate the new interests**

The process of accommodating the new regulatory framework is illustrated by the changes in the organisation of pharmaceutical sector collective action. There was a significant reformulation in business representation after the crisis in the pharmaceutical sector in 1999. Additionally, given the massive negative media attention, it was necessary to restore communication with civil society, government and academia.

At the suggestion of Jose Serra, generic manufacturers created a new business association in 2001, Pro-Genericos (Brazilian Association of Generic Drug Manufacturers), which was slowly taking shape. In 2003, Pro-Genericos gained an important staff member, the former director of ANVISA's Department of Generic Drugs, Vera Valente, who joined the association as Executive President. Valente has a bachelor degree in law, extensive experience in public management and was responsible for implementing all the initial stages of generic drug regulation in Brazil.

With the end of Fernando Henrique's administration they [generic drug producers] invited [Vera] to join Pro-Genericos. [Describing her work at Pro-Genericos]: That is publicity with doctors, pharmacists and to keep the mood of newspapers' interviews, disseminate [generic drugs] to society. Then 90% of work at Pro-Genericos was to give seminars, interviews, produce publicity material to drug retailers, to pharmacists so they understand their role and relevance in sales behaviour (Interview with local pharmaceutical industry informant A 2009).

This information was also corroborated with documentary evidence. A number of newspaper articles were culled citing Pro-Genericos activity in providing market intelligence data about the sector performance, reacting to attempts to disqualify the quality of generic drugs, providing information to the mass public about generic

drugs and among others (cf. Valentina Meyer Consultoria & Comunicação 2001; Gazeta Mercantil 2006a; Tribuna do Norte 2007). As the governmental campaigns to stimulate the generic drug demand shrank, in 2003 Pro-Genericos launched a US\$ 1.5 million dollar mass media campaign to inform health professionals and the population about these products (60% of this investment was financed by local producers) (Gazeta Mercantil 2003a). Furthermore, Valente strongly advocated for health insurance coverage of generic medicines. In Brazil, health insurance companies are not required to cover expenses with medicines. Furthermore, it was also under her leadership that Pro-Genericos began a strong counter-reaction to intellectual property extension. For instance, in a litigation between the French pharmaceutical manufacture Sanofi Aventis vs. the National Patent Office (INPI) for patent extension of Plavix, Pro-Genericos assisted the INPI, bringing elements of access to medicines, price reduction and the impact of generic medicines to the trial (Andrighi 2010). As we shall see later on in this chapter, Pro-Genericos has become an important player in defending the status quo of generic drug regulation, representing a counter-balance to innovator firms' preferences and intellectual property affairs.

Additionally, an important adjustment in the pharmaceutical sector post-generic drug reform was the extinction of Abifarma in April 2002. Abifarma had been one of the most influential representatives of the sector for more than 50 years. During the negotiations to introduce a generic drug law in 1999, Jose Serra and the president of Abifarma, Jose Eduardo Bandeira de Mello, had constant public disagreements, exposing the sector as a whole. Furthermore, because Abifarma's members were both national and multinational firms, there were frequent internal conflicts to define the Association's strategies on controversial issues affecting local and foreign capital. This internal divergence was limiting the association's ability to negotiate with the government. As Abifarma was unable to represent the new interests of pharmaceutical industries, a new association was created in June 2002, the Brazilian Federation of Pharmaceutical Associations (Febrafarma). Rather than clustering pharmaceutical firms, Febrafarma was a group of associations with the responsibility of unifying the voices of pharmaceutical sector, passing the controversial topics to



the respective segment, e.g. generic drug, innovator or local industry interests. “The government had segmented the sector. For some negotiations invited one association and excluded the other. We noticed that it was necessary to create an institution to speak for all of them. So, we created Febrafarma, representing all the associations” explained Nelson Libbos, former associated of Abifarma (Libbos in Sindicato da Industria de Produtos Farmaceuticos no Estado de Sao Paulo 2006: 68). A local pharmaceutical businessman, who participated in this reorganisation, commented this decision:

National and multinational firms sewed up an agreement to create Febrafarma. We, nationals, Alanac, knew we weren't majority or we are not majority [...]. It took two years of debate and we got to the point that we should make Abifarma extinct, not Alanac and not Interfarma. Why? In some issues there was an evident disagreement. Then, when there was a dissent topic each association would work by itself, while the common points Febrafarma would represent the sector. We knew we would not be majority within Febrafarma, we nationals, so we said “[...] Any negative vote is enough to define what a dissent topic is. Consequently, Febrafarma won't speak about that topic and will pass on to the associations”(Interview with local pharmaceutical businessman A 2009).

Aggregating the voices would strengthen the pharmaceutical sector, making policy advocacy more efficient. Although Febrafarma aggregated 15 associations of pharmaceutical sector (representing 267 pharmaceutical manufacturers), only three associations were eligible to vote: Alanac, Interfarma and Sindusfarma<sup>49</sup>. The common advocacy agenda refers to some regulatory affairs, price control, taxation, industrial policy and others<sup>50</sup>. A newspaper published an article suggesting that the former president of Abifarma, Bandeira de Mello, be set aside as his image had become associated with opposing generic drug policy (Valor Economico 2000).

### **Adjusting similar drugs and reinforcing the path**

In 2003, ANVISA proposed a new resolution establishing that all similar producers should also present the same bioequivalence tests as generic drug producers when

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<sup>49</sup> Pro-genericos is represented within Sindusfarma

<sup>50</sup> It is interesting to note that the headquarters of Sindusfarma in Sao Paulo also aggregate Febrafarma, Pro-Genericos and Abiminp (Brazilian Association of over the Counter Drugs). It is argued that this arrangement reduces an office's maintenance cost. However, when questioned whether the aggregation of these distinct interests in the same office would have some impact on their advocacy plans, only one business representative showed some discomfort, while all the others were pretty satisfied with this arrangement.

registering a product or in renewing its registration and that, by 2014, all similar products must be adjusted (Resolution 133 and 134 – 2003). Although there is a semantic distinction between the test names – similar drug resolutions mention a relative bioavailability test, while the generic drug resolution names a bioequivalent test – the pharmacological requirements are the same. Note that, as opposed to generic drugs that must be commercialised by an INN, similar drugs are allowed to present a brand name. Thus, this would put Brazil in an awkward situation, with four pharmaceutical products in the market: innovator product, generic product, similar product (not bioequivalent) and similar product (bioequivalent). Besides being beaten by the Intellectual Property Act and the Generic Drug Act, now local producers would have no other option than to adjust their products to fulfil bioequivalence requirements (although they would still be allowed to use a brand name). Relevant to this study is how the Ministry of Health and local producers interpreted and reacted to this proposal.

A draft of these two resolutions was sent to the Ministry of Health in 2003 for appreciation. A working group was created to debate 35 resolutions proposed by ANVISA. A former Ministry of Health official who participated actively in this working group recalls that, after two months of debates, they decided not to approve the similar drug resolution in the way that it was presented (Interview with government official B 2009). They suggested that conversion of similar drugs into generics should be incremental and be in the long term, looking first for products with narrow therapeutic ranges to give time to producers to adapt. Besides, they understood that bioequivalence tests are not the sole criteria to define the quality of medicines and this would increase the manufacturing costs of medicines. However, during the period of writing up the report, there was an intervention of ANVISA's president to convince the Ministry of Health that the resolution should be approved as it was proposed, i.e. unaltered and against the working group decision (Interview with government official B 2009). When questioned on the role of local pharmaceutical industries in this debate, this government official commented:

What happened was that [local] industries adapted to this regulation. Since 2003, similar drug producers adapted to this definition. [...] Indeed we had companies that had problems,

companies that are having problems. But, the segment as a whole took the political position to adapt. [...] Alanac adapted and did not oppose. Febrifarma was sympathetic. [...] Certainly, I was furious with them at that time. At that time I guess the decision to adapt was strategic to national producers so they wouldn't have to face questions about the quality of its products (Interview with government official B 2009).

Note that, even after the enactment of the Generic Drug Act, there was still room for local industrialists to maintain their production of similar drugs. However, the introduction of resolutions 133 and 134 not only reinforced the decisions taken during Serra's administration but expanded them, forcing all off-patent pharmaceutical products into providing bioequivalence tests. In December 2004, ANVISA suspended the registration of 130 similar medicines and cancelled the production of 30 similar medicines that did not comply with the new regulatory requirements (Gazeta Mercantil 2004). This decision affected 71 local firms (including 27 industries affiliated at Alanac), 10 multinational industries and 9 public laboratories. In 2007, a new resolution was published expanding the requirements to register similar drugs in Brazil (RDC 17/2207) (ANVISA 2007). The founder of a similar pharmaceutical industry commented:

Generic drugs didn't help me at all. By contrast, it harmed and still harms me [...] It is not just generic drugs that are required bioequivalence. According to the Brazilian legislation, even similar drugs, when renewing its registration, are required to provide bioequivalence tests compared to a reference medicine. So, I got several products that had a higher bioavailability of the product, i.e. I produce this product in a way that is better absorbed in the human body than the reference product and I had to worsen my product just to be equal to its reference version. [...] a generic drug is always equal to its reference version but never better. I cannot make my product better or it won't be bioequivalent and, not being bioequivalent, I cannot renew my license. (Interview with local pharmaceutical businessman A 2009).

Although some local producers were clearly dissatisfied with the decision that eliminated their products from the market, they opted not to voice their opinions against it (there was no record either in interviews or in newspaper articles of attempts to reverse or block these resolutions). As the government official mentioned, there was a movement of adjustment to the bioequivalence requirement. Furthermore, in 2003 the generic drug sector was already experiencing an extraordinary evolution. Market data highlighted the leadership of the national industry in this sector and the reductions on the price of medicines associated with it. For instance, in 2003 there were 37 national industries producing generic medicines,

with a market share of 75% in sales (Gazeta Mercantil 2003; Valor Economico 2003; Gazeta Mercantil 2003a).

The increasing success of the generic drug market affected similar drug producers. Although it would still be beneficial for them to contest ANVISA's resolution 133 and 134/2003, their chances of success fell considerably as more industries began to adapt. As the 2000s progressed, Alanac and other similar drug producers provided several declarations that similar products were also adjusting to provide bioequivalence tests: "the efficacy and safety of similar medicines produced and commercialized in the country are assured by pharmaceutical equivalence and relative bioavailability tests". It continues to: "most similar [drugs] have passed these tests, which are the same that generic medicines present, and until 2013 all similar drugs will have to be tested" (Alanac 2008). In 2006, the local pharmaceutical firm Ache (the only Brazilian publicly traded pharmaceutical company) bought Biosintetica, one of the leaders in the generic drug market. Ache has historically invested in similar drugs, but by acquiring Biosintetica it also reoriented its business plan toward the generic drug sector (Valor Economico 2006).

It is important to emphasise that, by 2014, all similar drugs must be adjusted to provide bioequivalence tests, which will require the government authorities to rethink the regulatory rules for commercialising pharmaceutical products. First of all, if similar manufacturers fulfil the same technical requirements as generic manufacturers, then similar products should also be considered interchangeable with an innovator drug (the same as generic products). Second, technically similar drugs will be a generic version with a brand name. In the United States and other developed countries, this is currently known as branded-generic drugs. This will also require these similar drug producers to rethink their business strategies and adjust their identity to (brand name) generic drug manufacturers. To conclude, in the words of a former similar drug producer that adjusted to the generic drug legislation:

You cannot have a first class product and a second class product. [...] With the generic drug legislation [...] you had an enormous amount of products in the market that did not provide bioequivalence. Brazil will have to abandon the definition of similar drug. Because with bioequivalence done at the same basis, you put an end in this market (Interview with local pharmaceutical businessman B 2009).

### **Framing the generic drugs: access to safe and efficient medicines**

Particularly important for this study is how local industrialists adapted their preferences to fit the generic drug regulation. As the theoretical chapter of this thesis suggested, preferences can be assessed by looking at how actors frame their claims and this can be observed empirically by looking at the content of their discourse and demands. As presented in the previous chapter, local producers used to defend vehemently their rights to use a brand name and were pretty uneasy about introducing new technical requirements to register off-patent medicines. Paradoxically, nowadays local producers account for 88% of the generic drug market in value. They present themselves as government partners to increase market competition, reduce the cost of medicines, and improve the quality of drugs (cf. Finotti 2009a); some of the biggest challenges are being faced by electors-consumers. These local generic manufacturers connect their demands to two policy domains: industrial development and production of high quality off-patent medicines. They have established a link between the new stringent regulatory rules, successful performance of national pharmaceutical firms and affordable quality of medicines. This suggests that local producers not only internalised the discourse that the bioequivalence test is a concept of quality control, but also began an aggressive dissemination of this normative frame, reinforcing the path of the Generic Drug Act. Looking at local producers' demands after the generic drug reform helps illustrate how preferences are endogenous rather than fixed, i.e. adjustable to the policy process. One of the current demands of generic manufacturers is to assure that prescription of medicines must be done by the international non-proprietary name or the Brazilian non-proprietary name:

[...] another important challenge to overcome barriers of access to medicines is related to the behaviour of medical class. It is essential health professionals use the generic name when prescribing medicines, as a way of assuring an economic feasible treatment to their patients, which at the same time assures its safety and efficacy (Pro-Genericos 2009a: 16).

The exclusion of the use of a brand-name on generic drugs labels is perhaps one of the main examples of how pharmaceutical firms changed their preferences after the

reform period. The core element of the Presidential Decree 793/1993 was to exclude brand-names of similar products, which both local and multinational industrialists reacted vehemently against, as was discussed in the preceding chapter. The advertisement of a brand name product is a key component of a pharmaceutical business, which usually focuses on fostering the credibility of the product (cf. Booth 1996). This quote, from the document that presents the institutional profile of Pro-Genericos, highlights the pharmaceutical firms that opted for the generic drug business, adapted to the regulatory process that mandated that they should exclude their brand names in order to commercialise these products in Brazil.

Furthermore, generic drug manufacturers have reiterated in policy relevant forums (such as Congressional hearings) that bioequivalent generic drugs are an important tool for securing access to safe and efficient medicines. One of the core demands of Pro-Genericos is that public purchase of medicines should respect the Generic Drug Act. As we have seen in the first section of this chapter, public purchase of medicines by the Unified Health System has privileged similar drugs instead of generic drugs, given the requirements of the public procurement legislation. Pro-Genericos have actively advocated for a reformulation in the public procurement law, which is under discussion in Congress.

In 2004, the Federal Deputy Walter Feldman (PSDB/SP) proposed a bid, number 3536, suggesting that public procurement should take into account – besides the regular requirements of Law 8666 - the certificate of Good Manufacturing Process and bioequivalence tests. Little is known why Deputy Walter Feldman decided to introduce this bid, however Pro-Genericos have been actively advocating approving this legislation in Congress. The president of Pro-Genericos, Odinir Finotti, commented in a public event, “the Law 8666 forces the public manager to purchase by the lowest price. But there is a limit to where the generic drug can go in terms of price, crossing that it would put at risk the quality of the product we defend”. In the document “Pro-Genericos: institutional profile” (Pro-Genericos 2009a), the association placed public procurement of medicines as one of its core challenges. It

reinforced the imperative need to take into account ‘quality of medicines’ to secure safety and quality of medicines provided in the Unified Health System:

The criterion of public purchase of medicine is also on the agenda of the challenges of generic industries in the Brazilian market. The sector believes that imposition of quality control criteria, according to the Brazilian sanitary legislation, in the public purchase of medicines is essential to society as a whole. Besides price requirements, it is necessary to also include requirements of bioequivalence tests and therapeutic equivalence in the public procurement, assuring safety and efficacy of medicines consumed by the users of the Unified Health System (SUS) (Pro-Genericos 2009a: 16).

This evocative language highlights the quality value attached to bioequivalence drugs. However, this linkage has been challenged by some groups of society as unnecessary and raises the debate as to whether this regulatory requirement is not just a manoeuvre to reduce competition of off-patent medicines (this is elaborated in the next chapter). Regardless of the internal motivation, which is not possible to observe empirically, indeed this discourse has a clever strategy as there is no room for policy discussion about the merits of quality control, nor space for support in the direction of “poor quality drugs”. As the local industries began to adapt, they highlighted themselves as producing high-quality drugs as much as innovator companies, providing a better product to consumers and contributing to access to medicines. In every public event assessed by this study, Pro-Genericos emphasises the centrality of bioequivalent generic drugs to as a certificate that medicines are safe and effective, linking generic drugs as to a major societal concern (access to medicines) and thus building a social image. Representatives of generic manufacturers also linked the generic drugs to industrial success that helps Brazil’s economic development:

The Generic Drug Act contributed significantly to local capital pharmaceutical industries, as they could effectively improve and develop qualitatively and qualitatively. National firms have done an interesting investment in know-how, technology, knowledge; such as that today they can compete equally in any international market. In other words, the regulation led firms to operate in another level, a higher level. [...] In this sense, never in the history of the pharmaceutical sector in Brazil have you ever seen the situation we have today (Finotti 2009a).

Additionally, I challenged a Brazilian industrialist to imagine a scenario where the regulatory requirement of bioequivalence was reversed and, if that could be possible. He vehemently reacted:

I think this is an enormous incoherence, in the counter direction of any global wave. [...] You have some standards that are basic in legislation of medicines. If a similar drug is not bioequivalent, then it should be considered a new product or a second standard product. Unless a similar drug has an incremental gain in pharmacotechnology [...] that represents a new product, subjected to a patent and everything that involves a new product. I would tell you that change the Brazilian legislation is an utopia. I believe that ANVISA would not allow this because it is to play against 10 years of a discourse and against what is happening in the world. That means that it is very positive that Brazil follows these standards because there was a monumental increase in the quality of local pharmaceutical companies, which can now compete equally in any part of the world, can export its products. So I think that to return to this discussion is to return to a discussion that in my opinion is absolutely empty (Interview with local pharmaceutical businessman B 2009).

What these two industrialists suggest is that there is a consensus that off-patent products must be equal to their innovation versions and according to them. This is not to say that the international norms diffused by WHO or the American Medicine Regulatory Agency (FDA) have driven Brazil's policy, but these quotes highlight how the national institutional context mediates this process. Observe the shift in the discourse of national industrialists compared to the antecedent period, where local firms had demonstrated strong concern with the magnitude and the pace of the reforms in the pharmaceutical sector. As pointed out in the previous chapter by a government official that participated in the debates of the generic drug reform, this group was extremely opposed to virtually all aspects of the generic drug regulation. Consequently, the fact that these industrialists are now strong advocates of this regulation also highlights how their preferences have adjusted in the course of the policy process. In turn, the inclusion of bioequivalence tests in the Brazilian norm reinforces the path of international generic drug regulatory practices. Another relevant aspect of this discourse is that the off-patent medicines' reputation and quality are bound together into the regulatory concept of bioequivalence. Thus, the negative image of pharmaceutical firms diffused during the period of generic drug reform is offset by this social image of a government partner that collaborates in the provision of public goods (in this case, medicines) and contributes in the industrial development of the country.

Again, this is not to say that they are not profit seekers but their utility is adjustable. For instance, instead of promoting the brand name product, generic drug manufacturers promote the credibility of their industry name. Furthermore, because



the Brazilian regulation allows a period until 2014 to adapt the similar drug products to the generic drug norm, many companies now use the same application dossier to register a generic drug and a bioequivalent similar drug (with a brand name) with the Resolution 133 and 134, 2003 mandate (Interview with local pharmaceutical businessman B 2009). The brand name product will be advertised at doctors' clinics with competitive prices and the generic version will go to drug retailers to be interchangeable. This discussion leads to the next section that deals with the commercial skills of Brazilian private entrepreneurs.

### **Using comparative advantage: commercial acumen**

Peter Evans noted, during the 1970s when he was conducting his research on industrial development in Brazil, that Brazilian pharmaceutical entrepreneurs are good businessmen (Evans 1979). This section shows how local pharmaceutical entrepreneurs saw possibilities to adjust to the regulation and took advantage of this market opportunity to redefine their business in order to fit the new institutional context, thus redefining their policy preferences and demands to the generic drug norm<sup>51</sup>.

The study of Abreu (2004) on the competitiveness of the Brazilian generic pharmaceutical industry suggests that access to the distribution chain was crucial to the success of local entrepreneurs in this sector. A large proportion of Brazil has access to medicines through out of pocket spending, thus drug retailers play an important role in the provision of medicines (Frenkel 2008; Frenkel 2008a; Pinto et al. 2010). Brazil has more than 60,000 pharmacies (more than twice the number recommended by the WHO) (cf. O Globo 2009b). To introduce a product on the pharmacy's shelves and deal with the complex pharmaceutical distribution chain there is a business acumen in which local firms have large comparative advantage (Abreu 2004). This opportunity also facilitated the possibilities to adjust to the reform and help explain their advantage against large multinational generic drug corporations. Furthermore, a representative of the pharmaceutical sector mentioned

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<sup>51</sup> A recently published newspaper article presents an interesting profile of the founder of EMS pharmaceutical industry and his commercial ability to survive in the generic drug sector, declining several merge/acquisition proposals (Valor Economico 2011)

two examples of managerial failure of multinational firms attempting to enter into the Brazilian market, but which have also contributed to give market advantage to local firms. The Indian firm Rambaxy, which brought a foreign executive with little knowledge of the Brazilian marketplace, and the Canadian Apotex, which was run by an executive with experience in brand-name drugs, both had little experience with the particularities of the drug retail network and distribution chain in Brazil and failed to encounter a commercialisation channel (Interview with local pharmaceutical industry informant A 2009).

A second explanation for the limited participation of multinational firms (*vis-à-vis* local firms) in the generic drug sector was their delay in entering the Brazilian market and this is also a product of the uncertain institutional setting during the reform. The interviewee commented that these multinational firms were flirting with Brazil and were unsure as to when would be the best time to enter the market. By deciding to observe the evolution of the market, they lost the opportunity (Interview with local pharmaceutical industry informant A 2009). In other words, as international firms were agnostic of market penetration of generic drugs, they decided to observe from the outside or cautiously join local pharmaceutical firms through joint-ventures before entering into the generic drugs market (*ibid*). This initial behaviour of foreign firms resembles the second postulate discussed in the theoretical chapter that refers to uncertainty (Hall 2005: 134). The generic drug reform created an unstable environment. As national firms began to adapt to the new institutional context and succeed in the generic drug business they reinforced the path, thus inducing other firms to behave accordingly.

Recently, there has been a movement of research-based firms into the generic market, particularly emerging markets such as Turkey, Russia and India (The Economist 2008; The Wall Street Journal 2008; Financial Times 2009; IMS 2009). With the consolidation of the generic drug sector in Brazil, the country also became a business target for these companies (O Globo 2009; Wall Street Journal 2009b). Furthermore, many multinational pharmaceutical firms are redirecting their investments from developed to emerging markets, and are keen to increase middle-

class demand for medicines (The Economist 2008; The Wall Street Journal 2008; Financial Times 2009; Financial Times 2009a; Wall Street Journal 2009b; New York Times 2010) [this phenomena was also observed by Quental, Abreu *et al.* (2008: 625) and Abreu (2004)]. The decision of research-based firms to join the generic drug market and the success of multinational generic drug firms (e.g. Indian and Israeli firms) in the global arena is an interesting phenomenon, but it is not the aim of this study to analyse their behaviour. What is important for this thesis is the fact that international firms considered Brazil as a business prospect, which may be associated with the opportunities created by local pharmaceutical firms. The fact that international firms rely on the success of local firms to enter into the Brazilian market (whether through merging/acquisition or joint ventures) not only stabilises the path of generic drug reform in the country but also illustrates how multinational firms have adjusted their preferences from innovation to production of copied medicines.

There are three examples of the movement of research-based firms into the generic drug sector in Brazil, creating hybrid pharmaceutical industries, with both generic and innovator portfolio (and consequently multiple preferences and demands). First, Novartis was one of the first research-based companies to develop a generic division (Exame 2005; The Financial Express 2005). Novartis adopted an aggressive strategy to gain the pharmaceutical market in Brazil. By introducing Sandoz and merging with the German Hexal (established in Brazil since 2001), Novartis increased their generic drug portfolio to 170 medications. Its market increased from US\$ 30 million in 2004 to US\$ 80 million in 2005 (Exame 2005). A second example is Sanofi-Aventis, which acquired one of the prosperous Brazilian generic drug industries, Medley, in May 2009 for US\$662.8 million. In a note the French pharmaceutical group mentioned: "This acquisition will enable Sanofi-Aventis to reinforce its number one ranking among pharmaceutical companies in Brazil, with a total 12% market share. Sanofi-Aventis will become the leading player in the field of generics in Brazil and in Latin America" (Wall Street Journal 2009b). The third example is the American Merck Sharp Dohme. The Director of External Affairs in Brazil commented: "We don't work with generic products worldwide and neither in Brazil.

Although Merck nowadays have a strategy to emerging markets, we are evaluating the possibility of having what we call branded generics or branded products” (Sanches 2009). There is an evident reorganisation of the generic drug market, increasing the participation of foreign capital in the Brazilian generic market (Gazeta Mercantil 2009; O Globo 2009). The effects of these hybrid firms are afoot and yet to be assessed, which is beyond the scope of this study.

### **Multiple interests: the intellectual property debate**

As we have seen so far, the generic drug policy brought about an extraordinary improvement to national industrial units, which prepared these firms for the expansion of their business in the research and development of new uses of known pharmaceutical products, for example. These are known as incremental innovations. Shadlen (2010), using data from the Brazilian Innovation Survey, suggests that investment in research and development by local firms increased significantly between 2000 and 2005 (344% in pharma-chemicals and 226% in pharmaceuticals). Data collected in the generic drug firm’s website also reveal an interest in R/D. *Incrementtha PD&I* is a joint venture arm of Biolab and Eurofarma, two leading local generic drug industries engaged in research and development of both incremental and new molecule products (Eurofarma 2011). EMS Sigma Pharma, a leader in Brazil’s generic drug market, has the most modern centre for research and development in Latin American and has invested nearly US\$ 13 million in R/D since 2002 (Globo 2011). Coinfar (*Consortio da Industria Farmaceutica*) is a joint venture between three national generic drug industries, Biolab, Uniao Quimica e Biosintetica; founded in 2005, it has been engaged in the research and development of analgesic and anti-cancer products (Rezaie et al. 2008). Shadlen (2010) also points to the evolution of patent application at the INPI, where Brazilian patenting activity in pharmaceuticals increased by 300% between 1994 and 2005 (among these 50% only in 2001-2003).

Additionally, since 2003 the Brazilian government has made efforts to stimulate pharmaceutical research and development activity in Brazil, which largely benefits national producers. During the Competitiveness Forum for the Pharmaceutical Chain

Production, which met between 2003 and 2006, pharmaceutical sector representatives assisted the government in identifying the bottlenecks to the sector's expansion in Brazil (Brasil 2003). As Brazil is highly dependent on the import of raw materials to produce medicines (active pharmaceutical ingredients), this was identified as one of the priority areas for investment of the Industrial, Technological and External Trade Policy (PITCE) (Brasil 2003). Several important political decisions were taken as a result of this discussion: sectoral funds, such as a credit line within the National Development Bank (BNDES) to pharmaceutical industries (Profarma) (BNDES 2009); two legislations were approved by Congress to stimulate innovative activities in Brazil: The Innovation Act (Law 10.973/2004) and Goodwill Act (Law 11.196/2005). These legislations created mechanisms for financial, technical and managerial support for innovative enterprises. Furthermore, they focus on the strategic partnership between universities or technological institutes and enterprises; technology-based entrepreneurship; incubators and technological parks; hiring of academic researchers by the private sector (cf. OECD 2010). Additionally, in 2007, when the Ministry of Health launched the *Mais Saude* (More Health Programme), which focused on the Health Industry Complex, the government pushed forward initiatives to stimulate research and development in the pharmaceutical sector in Brazil. There was a reformulation of the BNDES programme, with the expansion of the credit line to stimulate research and development (Capanema et al. 2008).

Thus, an important dimension of local industry's identity is their position on the intellectual property debate. Intellectual property regulation is relevant for this study as it can limit or facilitate the introduction of market competition, and thus cannot be ignored. However, it is important to note that this is a policy arena closely related to trade policy, but with overlapping agendas to generic drug regulation, as decisions in IP can affect the supply of off-patent medicines. So far, this chapter has presented arguments of technical requirements to register and market a generic drug that are debated normally within the Ministry of Health and National Sanitary Surveillance Agency. Now it turns to elements of trade policy, where the arena is broad, including the three branches of government (Congress, Judiciary and Executive government

and its departments). As discussed in the theoretical chapter, this thesis supports the argument that political actors have multiple interests (at times conflicting interests); as they weigh up one side of their preferences, this also asserts one dimension of their identity more strongly than the other. In other words, a gain in intellectual property capabilities would suggest conflicting interests of local producers at the same time as having to secure policies that benefit their generic drug business, while advocating for revisions in the patent system to accommodate their new innovative capabilities. For example, the study by Shadlen (2010) suggests that, as the Brazilian pharmaceutical sector gains new capabilities, it could alter their policy preference: from advocating for policies to facilitate the use of, and access to, knowledge, to advocating revisions in the patent system to accommodate incremental innovations. As a consequence, Shadlen argues, this could possibly erode Brazil's celebrated health-oriented intellectual property coalition. Similarly, the study by Kunisawa (2009) suggests that prohibitions against the patent of incremental innovation could harm local industry as this is an area where national industry may have a chance to generate new technology.

Nevertheless, my intention here is not to analyse the contestation over intellectual property per se as this could be a topic for another study (cf. Hasenclever et al. 2008; Kunisawa 2009; Shadlen 2009; Shadlen 2009a; Shadlen 2010). The analytical effort is to assess how, when and on which issues the intellectual property debate affects the generic drug regulation, which is not an easy task given the fuzzy line between these two arenas. During field research for this study there were three major issues on the intellectual property agenda in Brazil in which generic drugs appeared in the debates. The first is related to patent extension, or the pipeline mechanism; the second relates to the criteria for patent protection (e.g. second medical use); and the third relates to the procedure for registering a patent in Brazil. The position of local pharmaceutical producers on these three controversial issues shows how they embraced the identity of generic drug manufacturers, but also illustrates how their advocacy activities reinforce the path of generic drug policy. Similarly to Shadlen and Kunisawa, I also acknowledge that local producers have acquired new capabilities in research and development, which has added a new aspect to their

“preference function”. However, there as we shall see, there are several reasons to believe that their new skill has not been sufficient (yet) to alter their policy preference regarding intellectual property affairs, nor their identity as generic drug manufacturers.

### **Pipeline mechanism**

Some research-based pharmaceutical firms have claimed the rights to extend their products patent protection based on Articles 230 and 231 of Brazil’s Law 9.279/96 (Brasil 1996a), which is known as the “pipeline patent”. This mechanism refers to a “validation in Brazil of a patent issued abroad, ratifying the examination conducted by the foreign patent office, provided that the product covered by the patent application was not made commercially available” (Kunisawa 2009: 300). This means that, for one year only (in 1997), the INPI revalidated pharmaceutical patents granted in foreign countries<sup>52</sup>. For example, a patent issued for the first time in 1990 in the UK and recognised in Brazil in 1996 (date of IP law) will expire in 2010 in both countries, i.e. 14 years in Brazil and 20 years in the UK. Innovator companies argue that some pipeline patents lasted less than 20 years in Brazil; if this was so, they would have the legal right to extend it. Between 1996 and 1997, approximately 1,182 pipeline patents had been requested in Brazil; among these four were HIV/AIDS medicines (Folha de Sao Paulo 2007; Estado de Sao Paulo 2008; Jurberg 2008). However, until 2000 only half of these were granted, while the others were still under review (Jurberg 2008). Consequently, and arguably, because of this delay in granting the patent, innovator companies could then request a patent extension to cover this backlog.

While in 1999 there was only one patent extension request in the Brazilian judiciary, in 2008 the Federal Regional Court, 2<sup>nd</sup> Region (where 90% of similar trials are decided) ruled 25 cases of innovator industries against the National Patent Office requesting patent extension (Folha de Sao Paulo 2007). The first patent extension contest in Brazil took place in 2006, when the French industry Sanofi requested a

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<sup>52</sup> It is argued that this mechanism was included in the Patent Act because Brazil had little expertise in analysing pharmaceutical patent applications. It is important to remember that, from 1945 to 1996, Brazil did not recognise pharmaceutical patents, thus it would have to build up expertise in this area.

patent extension for Plavix up to 2013. Plavix is a heart disease medication and the second leading drug sold in the world (Folha de Sao Paulo 2006). While Sanofi argued that there was a delay by the INPI in granting the Plavix patent, which could justify an extension of their patent rights, the Judiciary understood that the Plavix patent extension was granted in France in 2000 and Sanofi only proposed the law suit in Brazil in 2005 (Valor Economico 2006b; Barros 2007). The court understood that the problem resulted from the company's own delay in requesting the patent extension. The relevance of the Plavix case is two-fold: first, this was the first time that courts ruled against patent extension in Brazil, which established a precedent for further judicial decisions. Second, it was also the first time that Pro-Genericos directly assisted the National Patent Office in a legal trial as *amicus curiae*<sup>53</sup>. Amicus briefs are when someone volunteers to assist a court decision [for more information about interest group involvement in courts see Baumgartner and Leech (1998: 141-144)]. Similar to the INPI, which had to build up its expertise in pharmaceutical patent analysis, so also had the Brazilian judiciary. Courts were ill-equipped to deal with the overflow of intellectual property litigations. Abifina then created a study programme in 2003 and 2004 to diffuse this issue. It organised four international seminars with experts from different countries to educate not only the judiciary but other business associations. As a result of this exchange of information, Business Associations got on track of *amicus curia*, following the American and European experience in this strategy. Brazilian firms also began using *amicus* as a tactic to influence the government (Oliveira 2010).

In the case of Plavix, where Pro-Genericos filed an *amicus*, they brought elements of access to medicines, price reduction and impact of generic drugs to the trial. Pro-Genericos presented a study demonstrating that 14 pills of Plavix cost R\$ 135.00 (maximum price), and that the governmental purchase of Plavix represented an expenditure of R\$ 720,000 in 2005 and 2006. The association argued that generic

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<sup>53</sup> Although Sanofi questioned the participation of Pro-Genericos, as it could have economic interests involved, the Superior Court of Justice understood the association's interest was juridical besides the economic advantages that might be associated with it. According to the Court Ministry, Nancy Andrichi, the discussion that this trial referred to was the right to freely produce medicines, an issue that is above all juridical and by which the contestation is exclusively related to (World Health Organization 2010d).



drug competition would reduce the price by at least 35%, meaning that governmental resources would be better spent elsewhere and would also increase the population's access to this medicine (Valor Economico 2006b). Vera Valente, former president of Pro-Genericos, declared in a newspaper interview: "The decision of the Rio de Janeiro court is a watershed in patent extension affairs. Pro-Genericos does not question the validity of patent but the generosity of extending it, which is an absurdity". She declared that the relevance of this decision goes beyond patent rights: "the referee mentioned other relevant topics such as access to medicines, lower prices, monopoly of industries and public budget" (Valor Economico 2006b). Besides the case of Plavix, in 2006 alone there were a further 11 judicial trials where the local pharmaceutical industry or its associations were assisting the INPI (Valor Economico 2006c).

Since then, Pro-Genericos has been advocating heavily against patent extensions. These court decisions have been ruled favouring the INPI and local industries, which is slowly building precedents in refusing patent extensions (Valor Economico 2007)<sup>54</sup>. The association estimates that, if all research-based firms are successful in expanding their patents, the Brazilian population would spend around US\$ 367.65 million between 2007 and 2013<sup>55</sup> (Folha de Sao Paulo 2008). According to Pro-Genericos, in less than two years after the Plavix patent expiration the market for Clopidogrel (its generic version) more than doubled from 777.240 units sold in 2007 to nearly 1.500.000 units in 2009 (Pro-Genericos 2009). The generic drug version represents more than 60% of the market share in volume, with a price reduction of 57% (*ibid*). This reinforces the path of generic medicines in Brazil and the role of the generic drug association in keeping the government accountable to it.

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<sup>54</sup> To contrast these decisions, multinational firms have moved its judicial requests to Brasilia, instead of Rio de Janeiro, where these cases are usually decided. INPI's headquarters are in Rio, traditionally the TRE-RJ, the locus of the debate. With the regional tribunal less sensitive, lawyers have argued that legally Brasilia should be the locus of INPI. In Brasilia, INPI is represented by the General Prosecutors that have less experience in these cases than the ones in Rio de Janeiro, thus they might be more sympathetic to multinational firms' arguments (Valor Economico 2007).

<sup>55</sup> This estimate is based on the projections of sales volume of each product under contest until 2013 (excludes the inflation and currency variations) multiplied by the average/pill price and reducing 35% (according to the legislation, generic drug price must be at least 35% lower then its reference version).

### **TRIPS Plus agenda: polymorphs and second use**

In 2007, the National Patent Office (INPI) launched a series of meetings with representatives of the pharmaceutical sector to discuss a revision in their patent standards. The INPI officials decided to revise the technical requirements for patent granting after participating in an international Congress where several controversial topics were raised. Furthermore, representatives of the pharmaceutical sector also requested a revision in Brazil's rules (Interview with government official C 2009). The three revision meetings were organised with representatives of industrial segments of the pharmaceutical sector - generic, innovator, similar and public producers<sup>56</sup> - and took place between June and July 2007 (INPI 2010). Representatives of HIV/AIDS patients have expressed an interest in participating in these events, but at first the INPI demonstrated concern about the extent to which this group could contribute to the technical meetings. This controversy and the perception of AIDS advocacy on this matter is assessed in the next chapter.

There were two contentious topics on the agenda: patent of polymorphs and, second, medical use. Polymorphs relate to the ability of a solid material to exist in more than one form or crystal structure. This is important in the manufacturing of pharmaceutical ingredients as it may affect the bioavailability, manufacturing, and stability of the drug product (cf. Raw and Yu 2004). The second medical use refers to innovative therapeutic use of medicines already patented. Arguably, both could be classified as incremental innovation of existing products, thus subject to patent protection. Because these are provisions beyond the TRIPS requirements, they are usually referred to as TRIPS-Plus (which also includes the pipeline mechanism). The international agreement on intellectual property set minimum standards that each member country would need to implement to secure the rights of inventors; however, the expansion (or not) of this norm would be at the discretion of each government. For instance, much has been discussed about the US pressure to expand the IP rights through bilateral trade agreements with developing countries, for example Nicaragua, Jordan, and Mexico (Drahos 2001). However, up until the writing-up process of this

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<sup>56</sup> Detailed records of these meetings are available on the INPI website [www.inpi.org.br](http://www.inpi.org.br).

thesis, Brazil had not been engaged in any bilateral or regional trade agreement that could encourage a reformulation in the patent system (cf. Vivas-Eugui 2003; Mayne 2005). As noted, the decision to revise the scientific guidelines to assess patent requests was taken after the INPI officials learnt in an International Congress, through the experience of other countries, of the controversies associated with it. However, how and the extent to which this would be possible in Brazil would depend on the policy legacies and commitments in place in Brazil.

Defining the extent of innovation in these cases has proved to be a difficult task and a challenge for policy-makers at the INPI and ANVISA, thus this debate migrated to Congress. In late 2007, the Federal Deputy, Fernando Coruja, introduced a bill to eliminate patents for second medical use and polymorphs (Bill 2.511/2007) (a year later, another similar bill was introduced by Deputy Paulo Teixeira and Deputy Dr Rosinha – Bill 3.995/2008 and attached to the previous bill). Given the high level of disagreement around this topic, several public hearings were held in Congress to give an opportunity to all sides to express their views on the matter (Soares and Correa 2010).

One side of the debate, supported by the representatives of research-based firms (Interfarma and ABPI), understands that the patent of incremental innovation is important as it could stimulate industrial development in Brazil and give opportunity to local firms to recover the costs of their investment, thus creating an incentive to research and development. In contrast, critics such as national industry representatives (Pro-Genericos and Alanac) and AIDS activists, argue that these slight alterations are simply a way to extend patent protection of medicines and delay market competition. In the polymorphism debate, for example, Marcos Oliveira, Vice-President of Abifina, declared “Nobody invents polymorphs. What you discover is that under certain conditions of production you can have different polymorphs. This is a discovery [...] it has nothing to do with invention”. He concludes, “Today this is absolutely trivial. You get a molecule and send it to a laboratory and it will produce 10, 12, 15 or 20 different polymorphs out of the same molecule. So, there is no inventive activity” (Oliveira 2010). Furthermore,

representatives of local firms suggest that Brazilian firms would still need more time to expand their R/D activities to be able to benefit from these regulations. The Brazilian Association of National Pharmaceutical Industries (ALANAC) expressed their position against the patent of second medical use and polymorphs and supported Deputy Fernando Coruja's bill:

This matter [second medical use and polymorph patents] does not favour the development of national industry. By opposite, its permission would represent a huge drawback vis-à-vis the accomplishment that national industries have gotten, Brazil's development and the pharmaceutical industry [Alanac's position, represented by Carlos Alexandre Geyer, at the Commission of Social Security and Family of the Deputy Chambers] (Alanac 2009).

Finally, this position is also corroborated by Pro-Genericos. "Pro-Genericos and other institutions argue that if this product [resulted from a polymorphic alteration] has the same efficacy than the other, given that is the same product, then it should not be patented. [...] From our perspective it is not a new product", said a representative of Pro-Genericos in an interview for this project (Lobo 2009). He explained, "what is new is the process of production, and then you need to patent the process but it can not patent the product" (*ibid*).

The contestation around these topics involves not just segments of the pharmaceutical industry and patient advocacy, but also highlights a divergence between government departments (cf. Kunisawa 2009). Registration of pharmaceutical patents in Brazil requires a revision from the Patent Office, but also permission of a National Sanitary Surveillance Agency (ANVISA). Since 2001, ANVISA has also been involved in granting patents for pharmaceuticals in Brazil, a mechanism named "prior approval". The divergence between these two government departments is discussed in the following section. For now it is important to point out that, while ANVISA has adopted a strict interpretation of the patent legislation, the INPI has been more sympathetic of incremental innovation patents. ANVISA argues that "patent of polymorphs could led to monopolies that inhibit competition and also limit the universe of local inventors" (Soares and Correa 2010: 46). Contrastingly, the INPI is aligned with the arguments that patent of polymorphs could integrate Brazil with the global technology network (Soares and Correa 2010).

Finally, the Minister of Health, Jose Gomes Temporao, declared in an interview to a newspaper in 2008 that he was reluctant in accepting the introduction of the new patent mechanisms in the current patent system in Brazil (Valor Economico 2008). During the public hearing at the Chamber of Deputies in November 2008, it became clear that the Ministry of Health and Foreign Affairs was concerned that patent of incremental innovations could go against international debates in which Brazil has been leading, such as the Development Agenda of the World Intellectual Property Organization and WHO's Global Strategy in Innovation, Public Health and Intellectual Property (WHA 61.21) (Abia 2008). In other words, it was calling coherence from Congress, in that the government's orientation on this matter should be aligned with its international advocacy agenda. Nevertheless, in Brazil's democratic context, different groups engaged on the intellectual property reform have had the opportunity in Congress to express their perspectives<sup>57</sup>. The result of this deliberation is yet to be seen. Evidently, this discussion would also spill over into the Ministry of Industry, Development and Commerce that also sent a representative to this Congressional hearing. However, the meeting record suggests that the Minister of Health, Temporao, did not expand the position of his cabinet, but suggested that just the National Patent Office could not determine resolutions on patent of incremental innovation. It had to be discussed within an inter-governmental forum (Abia 2008).

In this sense, following the discussions in Congress, the Executive government also debated this topic within the Inter-Governmental Group for Intellectual Property meeting in December 2008 (Ministerio do desenvolvimento Industria e Comercio Exterior 2008). The executive government officials reached a consensus that Brazil would not support second medical use and polymorph patents as these revisions did not benefit the national industries, given the level of development that they encounter (Revista Facto 2009). Although this decision is not enforceable, it is a signal to

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<sup>57</sup> Less is known about how the Minister of Foreign Affairs (MoFA) deliberates on which direction to support on international debates (Montero 2005). For example, there are no frequent public hearings and much of the decisions are taken through ad hoc consultations with other Ministries and interests groups. Despite Brazil's international visibility on international health diplomacy, much this overseas agenda did not appear in the field research for this case study. In an attempt to understand the linkage between both, I have interviewed decision makers at the MoFA. When questioned about the debates presented in this section, they referred me to other ministries/government departments.

Congress and to societal actors that the Brazilian government is not sympathetic to patents for incremental innovation. During the writing-up of this thesis, the Brazilian Congress was still debating this matter.

This debate highlights important aspects of preference of pharmaceutical firms. While research-based pharmaceutical association (formed mainly by multinational corporations) frame their support to patent incremental innovations, arguing that this would foster the research and development capacity of local firms, the genuine representatives of local pharmaceutical firms (Alanac, Abifina and Pro-Genericos as the majority of their members are local producers) do not. They argue that some of these products that would require patent protection have no inventive novelty. Different government departments are more or less receptive towards each of these claims, while the INPI is sensitive to the necessity of clarifying the patent criteria in these cases. The other government department responsible for judging patent application, ANVISA, does not support these revisions. Given the controversy associated with this debate, Congress is now deliberating on which direction to take. Nevertheless, the preferences and demands of local producers in the polymorphism and second medical use suggest that these firms are still strong supporters of the right to replicate off-patent pharmaceutical products. In this sense, little has changed in this dimension of their preferences compared to the debates to implement the Patent Act in the early 1990s. However, advocating for a stringent patent protection system highlights a strong identity of local producers as generic drug manufacturers.

### **Procedure to register pharmaceutical patents in Brazil**

The previous chapter mentioned that one of the reforms in the patent system was the procedure to grant patent protection in Brazil, giving authority to the National Health Surveillance Agency to review patent applications. This arrangement is called “prior consent” (*anuencia previa*). Note that this is again a topic from the territory of intellectual property. However, “prior consent” could facilitate or limit generic drug competition by defining whether a patent could be granted or not. Consequently, it can also determine the timing for generic drug competition and, as a result, it is

important to assess the interpretation of the pharmaceutical sector actors to this arrangement.

In Brazil, every pharmaceutical patent request must be assessed by both the Patent Office and the Health Surveillance Agency. After the analysis by the INPI, which assesses the three patentability requirements (industrial application, new and inventive step), the application is forwarded to ANVISA, who revises the patentability requirements and assesses the relevant aspects of public health (e.g. the implications for public health). This means that the health surveillance agency has the power to veto the granting of patents in Brazil<sup>58</sup>. The role of ANVISA in the process of patent granting is arguable. In case-conflicting reports, a technical meeting is organised to resolve their analysis. If there is no consensus, patent applicants can fill an administrative or judicial appeal against the decision (Basso 2006). ANVISA has disagreed starkly with the INPI on issues regarding the procedures to approve pharmaceutical patents (Rodrigues-Junior and Murphy 2006; Guimaraes 2008; Kunisawa 2009; Shadlen 2010).

Since September 2001, and immediately after the reform, the Brazilian Intellectual Property Association (ABPI) has been advocating against ANVISA's prior consent on the grounds that the health surveillance agency does not have the technical expertise to assess patentability requirements, that its intervention duplicates the administrative procedure to examine patent application, and even questions the constitutionality of this procedure (given that, to be granted a patent, the product should present elements of invention, novelty and use, thus having less to do with its implications to public health) (Guimaraes 2008; Teixeira 2009). According to these advocates, all these requirements delay the examination process. Furthermore, because ANVISA has starkly disagreed with patent of second use and polymorphs, both ABPI and Interfarma argued that prior consent is harmful to the local

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<sup>58</sup> Alternatively, Cardoso's administration could have adopted a different strategy to assess public health implications in patent analysis. For instance, it could have detailed the legislation to clarify conflicting interpretations or revise INPI's parameters to spell out what could (or not) be patented. Given that article 229-C of the Patent Act was inserted through a Provisional Measure enacted by the President, there were no debates in Congress that could evidence the motivation to introduce ANVISA's participation in this process (Basso 2006; Kunisawa 2009).

pharmaceutical industry as it reduces the incentives for these firms to invest in incremental innovation (Raimundo 2009).

However, the perspective of prior consent could be harmful to the local industrial development if it is not shared by representatives of national industries. Looking at the position of Pro-Genericos, Alanac and Abifina (Brazilian Association of Fine Chemicals) on the Congressional hearings for the Bill 3709, local pharmaceutical producers seemed reluctant in advocating against ANVISA's role in assessing patent application. The president of Pro-Genericos declared in the meeting of November 2009:

In our understanding [...] and we speak here in the name of all Brazilians that use generic medicines. We understand that it would be prudent to continue these analyses [prior consent] very carefully. We - excuse my petulance - we believe that both agencies [INPI and ANVISA] should work together to find a way to harmonise the job of examining patent applications. We are saying (and everything is transitory) that... we understand that at this exact moment, taking into account how the country is now [...] it is good for Brazilian society to be careful with this. [...] [Prior consent] is in the [patent] law and we want to keep it. [...] We want the law to be respected (Finotti 2009b).

Similarly, in January 2011 the government department that provides legal advice to the Executive Government, the Solicitors General (*Advocacia Geral da Uniao*), issued a statement against ANVISA's prior approval consent (Gazeta do Povo 2011). The president of Pro-Genericos, Odinir Finotti, promptly reacted against it citing that, with ANVISA's assessment, the arguments for requesting a patent tend to be more solid, thus it is important to have an agency that deals with public health assessing technical aspects of patent requests (*ibid*). Furthermore, when questioned about the Bill 3907/2008, the vice-president of Abifina, Nelson Brasil, replied "Abifina's members understand that prior consent offered by ANVISA regarding pharmaceutical patent application is a legal duty that aims to fulfil national public health interests, that is why it should be maintained. With respect to the content of this legal regulation, Abifina has not established a final position" (Brasil 2010). This advocacy to keep the prior consent institutional arrangement also facilitates the expansion of generic drug products, as ANVISA has opposed grant patents to several medicines that were, arguably, underserved.



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This section has analysed the position of local producers and generic drug manufacturers in different intellectual property contestations. The evidence culled from newspaper articles, official documents and interviews with key informants suggest that these actors still have a strong identity of off-patent medicine producers. Their preferences and demands in different forums and aspects of intellectual property highlight that they are trying to protect their rights to replicate medicines, despite their recorded gain in innovative capabilities as suggested by Shadlen (Shadlen 2010). This author has pointed to the contradictions of promoting and encouraging research and development in this sector (particularly given that Brazilian firms are more able to perform incremental innovations) at the same time as securing the agenda of health-oriented intellectual property (as, for example, the prior consent arrangement). These findings further reinforce the concepts discussed in the theoretical chapter of this thesis, that actors have different and, at times, conflicting preferences. All the examples and conflicts discussed in this section suggest that the Brazilian government and the local pharmaceutical firms have a stake in expanding innovative capabilities and the generic drug market simultaneously. Their preferences and demands so far strongly indicate an identity and preference for expansion of generic drugs rather than revising the intellectual property status quo. Furthermore, these findings also highlight the importance of a qualitative study of actors' preferences, as a narrow approach (support vs. opposition to intellectual property) would miss this important aspect of the policy process.

## **Conclusion**

This chapter provides several reflections for this thesis. Framed as a government intervention to overcome a market failure, it is expected that government would have a strong role in stimulating and promoting these products in order to encourage a demand and supply. However, as this chapter has demonstrated, the Brazilian government has discontinued its strong advocacy for generic drugs, a fact that was

observed during the reform period, and the market demand is apparently fragile according to the information culled. It seems that the support of generic drug manufacturers has been crucial to preserve this norm throughout the 2000s. This is not to dismiss the role of ANVISA in enforcing the legislation, but to highlight how the advocacy of generic drug producers has been crucial in reinforcing and legitimising the path of the Generic Drug Act. This finding is relevant for the overall argument for several reasons. First, it reinforces how the alternative explanation, proposed in the first chapter on the diffusion of the World Health Organization, can provide guidelines on what would be done, but it is not sufficient to promote changes in domestic pharmaceutical regulation. The acceptance of local stakeholders is crucial in order to foster and legitimise these guidelines.

Second, this chapter suggests how the preferences and demands of actors are flexible and adjustable in the course of the interaction with the policy process, rather than being fixed and linear. Despite the initial resistance of local pharmaceutical manufacturers to the regulation of off-patent medicines, they have found opportunities to adjust and have successfully grabbed their place in the pharmaceutical sector in Brazil. Citing the representative of the Minister of Health's speech in a seminar about Patents and Generic Medicines in Brazil, the success of the generic drugs in Brazil is as a result of the dynamism and entrepreneurship of local businessmen (Guimaraes 2009). These producers had reorganised the interest groups' representation to fit the agenda of generic drug regulation, supported the bioequivalence requirement and the use of INN/BNN in different forums, used their business acumen to retail their products and were strongly opposed to several legislations to expand the intellectual property rights. All these highlight how their preferences and demands were adjusted to fit the new institutional context but, in turn, how they reinforce the policy path. To put it differently, had local producers not adapted to the generic drug regulation, would this policy have developed the way it did? As this chapter has demonstrated, despite Jose Serra's advocacy to bring foreign generic drug firms to Brazil to stimulate competition (Serra 2002: 295), multinational producers such as Apotex and Rambaxy were either suspicious of the potential of the Brazilian market and the stability of the regulatory norm or had taken failure

attempts to enter the market (e.g. problems in accessing the distribution channel). Thus, the support of local pharmaceutical producers is apparently crucial to the path of generic drug policy development.

Third, with respect to the content of lobbying activity and the structure of interest group representation, several reflections can be observed. This chapter has demonstrated different policy demands of generic drug producers, ranging from a preference for generic drug products in public procurement of medicines to opposition to the revision in the Patent Act and others. Pro-Genericos and other business associations have collaborated with government by providing information and educating government officials about technical aspects of pharmaceutical regulation. Particularly interesting is that their claims are usually framed as promoting Brazil's industrial development, but also partner with government in an effort to provide affordable and high quality pharmaceutical products. This is not to say that firms are not profit-generators, but that their preferences and the way they interact with government is more complex than the narrow approach to "utility maximisers".

Yet, on the complexity of preference formation, we have also seen that these producers have engaged in research and development of incremental innovation but also have been stimulated by government to do so. This might suggest the controversial decision on which direction to advocate for, whether to protect their generic drug business or advocate for expansion of the intellectual property protection to cover their incremental innovator products. Similarly, the Brazilian government has promoted and directed its attention to stimulate research and development of the pharmaceutical sector. As demonstrated in this chapter, the Ministry of Health in particular has launched an ambitious project to decrease the dependency of foreign capital in this sector. Decisions such as this might include giving priority to purchase products locally produced at the expense of cheaper imported versions, arguing that, in the long term, this will develop the industrial capacity of Brazilian firms. It is not the purpose of this study to discuss the merit of each of these options or uncover the inner motivation of these actors. What this

evidence tells us is that, by putting more weight and advocating more heavily for one of these sides, the actors highlight one aspect of their preferences, thus reinforcing one identity. In other words, local pharmaceutical producers in Brazil still have a strong identity of off-patent drug manufacturers, despite their recent expansion and gain in capability to carry out research and development. Similarly, the Brazilian government strongly indicates that it opposes a revision in the Patent Act and a commitment to carefully consider the public health dilemmas associated with it.

A final reflection is worth mentioning here as to why these local firms were able to adapt better to the Generic Drug reform than to the intellectual property legislation (which they also starkly opposed). The answer to this is not simple and is beyond the scope of this thesis (see the study of Shadlen (2009a) for a discussion on domestic political mobilisation on intellectual property in Brazil and selected Latin American countries). Nevertheless it is worth considering that, as opposed to the generic drug regulation, where there was a strong governmental commitment on the necessity to change the direction of off-patent drug regulation, the intellectual property debate remains much more controversial, opening up room for different preferences to be expressed. Besides, local firms had been historically limited in their research and development capacity. Thus, their opportunity to adapt to the generic drug regulation was higher vis-à-vis their chances to adjust to the IP institutional context.

In sum, this chapter assessed relevant aspects of the regulatory process of generic drug regulation in Brazil in the 2000s that explain the political stability of the reform and its effects on selected actors. The next chapter also explores the policy development stage but focuses on its unforeseen contingencies and the reaction of actors that had not been engaged in this debate to date.

## **6. Public production of medicines and HIV/AIDS activists: new actors in the generic drug regulatory process**

This chapter further expands the analysis of the regulatory process of generic medicines in the 2000s and turns now to assess the stakeholders that question the current architecture of the pharmaceutical regulation in Brazil. Normatively, the generic drug regulation is an intervention to overcome market failures, thus analyses of its effects tend to centre on government, market demand and supply. However, a process-tracing approach evidenced unintended consequences of this regulatory policy and the entrance of groups that were not engaged in the initial stages of the regulatory policy reform. Theoretically, this information provides reflections on the evolution of actors' preferences and highlights important aspects of structure of interest group representation in the pharmaceutical sector in Brazil. From a practical point of view, it raises concerns on the stringency of Brazil's regulatory guidelines.

There is an increasing apprehension among AIDS activists about the stringency of Brazil's regulation for generic medicines, citing that these rules might limit competition and undermine access to medicines. Similarly, public pharmaceutical factories have voiced their struggle to adapt to this norm for different reasons and questioned the necessity of such strict regulation. The decision to cluster these two actors in this chapter was for heuristic purposes. Both activists and the public pharmaceutical factories were less engaged in the generic drug reform but were apparently affected by this policy. Also, as seen in chapter 4, public pharmaceutical factories have a strategic relevance to the provision of AIDS medicines, thus combining these two stakeholders in order to facilitate the analysis and understanding of this aspect of the regulatory process. Because the time frames for chapters 5 and 6 are alike, interactions between these stakeholders are highlighted when necessary.

This chapter is organised as follows. The first section of this chapter analyses the effects of generic drug regulation on the public production of medicines, focusing on

the interpretation and reaction of public producers to this policy. This also serves as background information to the following section that assesses AIDS activists' preferences and demands. Much of the off-patent antiretroviral drugs supplied to the National AIDS Program are produced by public pharmaceutical industries, thus have a direct impact on the treatment of these patients. The second part deals with AIDS activists and assesses how they began participating in the pharmaceutical regulatory process, what their claims are and how this contributes to the path of generic drug regulation in Brazil. Similar to the previous chapter, their agenda and participation on the intellectual property debate is also assessed and compared to the findings of the previous chapter.

### **Public pharmaceutical industries**

While the previous chapter demonstrated how private local pharmaceutical industries have successfully adapted to the generic drug reform, this chapter discusses the struggle of public drug producers to adjust to it. Brazil has 18 public pharmaceutical industries (or laboratories) that supply most of the pharmaceutical assistance programmes. These public producers differ in their size, management and financial structure (Oliveira et al. 2006; Gomes et al. 2008). While some are attached to universities, others are federal and the responsibility of the state government. In 2003, public industries were responsible for supplying 84% of medicines purchased by the Ministry of Health; these four public industries (Farmanguinhos/Fiocruz, Furf-Sao Paulo, Lifal-Alagoas e Lafepe/Pernambuco) represented 75% of the supply (Bastos 2006). However, in terms of value, public suppliers represented 19% of expenditure, while private suppliers represented 81% (Lourenco and Chaves 2004). Public producers are also key providers of medicines to governmental programmes, such as Popular Pharmacy (Miranda et al. 2009; Pinto et al. 2010). All these highlight their relevance to the Unified Health System in Brazil.

There are repeated criticism of the production of medicines in public industries on the grounds that it is inefficient (cf. Kaplan and Laing 2005). However, the production of medicines in public industries in Brazil is justified for several reasons.

Firstly, Brazil has public pharmaceutical industries in different regions of the country and they are the most important suppliers of medicines to public health programmes (particularly for chronic diseases) (Oliveira et al. 2006). Secondly, these public factories can provide information about the manufacturing process and costs of production of medicines. The disclosure of this information allows the government to establish target prices and the knowledge of whether private laboratories are demanding a fair price for their patented medicines (cf. Valor Economico 2001a). Thirdly, if Brazil has the capacity to produce patented medicines, it also allows the government to make credible threats to issue a compulsory license when negotiating prices with patent holders (Cohen and Lybecker 2005; Flynn 2008; Nunn 2008). Note that the role of public laboratories is beyond the supply of cheaper medicines; it refers to their capacity in regulating the pharmaceutical market and serving as a strategic mechanism to negotiate price with patent holders.

Despite this strategic relevance, in the early 1990s public laboratories were struggling to keep their production capacity (Bermudez 1992). However, in 1994 the Federal public laboratory Farmanguinhos experienced a technical and administrative reform under the leadership of Eloan Pinheiro, a pharmacist with long experience working for multinational firms (Flynn 2008: 522). Additionally, during 1998 the Minister Jose Serra made important investments in Brazil's public laboratories and strategically expanded public production of antiretroviral medicines (Flynn 2008; Nunn 2008). He allocated nearly US\$ 40 million in modernising the production capacity of these industries to bring them into compliance with the new regulatory rules. This investment increased these public industries' production capacity by seven times (Hasenclever and al 2004). A further US\$ 100 million was invested between 2003 and 2005 (Bastos 2006).

This experience in producing AIDS medicines has increased public laboratories' capacity in reverse-engineering pharmaceutical products (Cassier and Correa 2003). Because imitators do not usually have complete information about a given drug manufacturing and synthesis process, it is necessary to rediscover the knowledge used to formulate this drug – this procedure is referred to as reverse-engineering.

Compared to the research and development investment and timeframe of discovering a new molecule, reverse-engineering is a relatively easier process but still implies the use of high technological capacity. This type of research is process-oriented instead of being product-oriented, which innovator companies are engaged with. Yet, both research strategies develop technological skills and the possibility of industrial development (see Evans 1979: 192 - footnote 5).

They [Brazilian chemists] did not have access to the knowledge that the owners of patented molecules held or transferred to their licensees. Nor could they rely on references in pharmacopoeia on the components of these drugs since they were not disclosed. These chemists therefore reinvented tests to identify drug components, consisting of reverse engineering to find their formulae and synthesis processes. The knowledge acquired exceeds the industrial capacities of the government laboratory which is equipped only to produce the pharmaceutical form of the drug (Cassier and Correa 2003: 105).

According to Cassier and Correa (2003), as public laboratories gain new capabilities in replicating innovator medicines, they have sought to take higher technological steps and embarked in research and development of incremental innovations<sup>59</sup>. Nevertheless, public industries still face enduring challenges to adapt to the pharmaceutical regulations introduced in the late 1990s (Cassier and Correa 2003; Flynn 2008; Gomes et al. 2008). One of the main challenges of public factories is to adapt to the regulatory rules such as Good Manufacturing Practices and Bioequivalence requirements. Until 2004, only four public producers received a certificate for Good Manufacturing Practices (Bastos 2006). But more controversial is the adjustment to provide bioequivalence tests (cf. PNUD 2006; Gomes et al. 2008; Hasenclever et al. 2008). It is interesting to note that, during the pharmaceutical reforms that took place in the 1990s, and particularly the generic drug regulation that is the core object of this analysis, the process tracing analysis has found that representatives of public pharmaceutical producers had limited participation in the discussions and the enactment of these reforms. An interview with a government official that had insider information about these factories

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<sup>59</sup> There are two considerations here. Farmanguinhos, together with Lafepe, are Brazil's most important public industries in terms of technological advancement. Anecdotal information suggests that after a change in the direction of Farmanguinhos in 2004 there was a brain drain in the research and development capacity of the institute. That being said, Farmanguinhos has engaged in further research and development of neglect disease medications; for example, a partnership with the DNDi (a non-profit organisation engaged in developing new treatments for malaria, visceral leishmaniasis, sleeping sickness, and Chagas disease) (see [www.dndi.org](http://www.dndi.org)).



suggested that they were concerned with the direction of the generic drug reform, particularly the bioequivalence requirement, but any attempt to question this was largely set aside by Serra's administration (Interview with public pharmaceutical factory informant A 2009).

Consequently, there are several reasons for the slow pace of public industries to adapt to the bioequivalence requirement. Firstly, and particularly problematic, is the fact that public pharmaceutical producers (similar to private ones) are not able to incorporate all stages of the manufacturing process. Their limited technological capacity to produce active pharmaceutical ingredients (API) forces them to obtain them from foreign markets such as China and India and, to a lesser extent, Brazilian private firms. Public purchase of API must comply with the Public Procurement legislation and contracts are awarded to the bidder with the lowest price possible (Law 8666/1993). Because of the lowest price criteria, it is argued that some of raw materials supplied to public pharmaceutical industries are very low quality (Gomes et al. 2008). Because these raw materials are frequently rejected by the Department of Quality Control, it needs to be reprocessed, leading to a delay and increase in the manufacturing process. For example, between 2003 and 2006 among the 34 batches of antiretroviral drugs, 28 (nearly 80%) were below the international industrial performance of 97% (Costa et al. 2008).

The problem with the quality of raw material limits not just the capacity of public laboratories to adjust to the sanitary regulation, but also impacts on timetable delays and production costs. For instance, to produce bioequivalence tests according to Brazil's generic drug resolutions, producers must fix no more than three raw material suppliers, but giving priority to firms in public procurement is forbidden by the Public Procurement Act (public institutions are not allowed to privilege goods/services suppliers) (Costa 2009; Oliva 2009). According to this legislation, public procurement must be carried out in public bids and respect the criteria of the lowest price. Thus, it is important to note that the difficulty of public producers to adjust to the generic drug regulation is beyond a matter of business strategy, costs or technical capacity. It is also obstructed by public administration rules (such as the

Law 8666). Given that public pharmaceutical producers are regulated by the same health norms as private pharmaceutical industries, by 2014 all medicines produced must adjust to bioequivalence requirements or else will not be allowed to renew their registration.

Secondly, public producers questioned the relevance of bioequivalence as a proxy of quality medicines. Because public industries have a long tradition of producing and supplying medicines to public service, it gave room to discuss the relevance of bioequivalence requirements (cf. Hasenclever and al 2004; Gomes et al. 2008). The argument is that these medicines are in use for a long time and have had their clinical performance validated already. Between 1996 and 2006, around 26% (sales) of the AIDS medications supplied to the National AIDS Program were produced by public industries (Costa 2010). Although there is no study about the effects (e.g. viral load resistance) of antiretroviral drugs produced in public industries on AIDS patients, many studies reported the significant improvement in life expectancy and quality of life of AIDS patients in Brazil (Esau et al. 2003; Marins et al. 2003; Hacker et al. 2004; Teixeira et al. 2004; Campos et al. 2005; Matida et al. 2005; Dourado et al. 2006). Furthermore, other health programmes, such as the tuberculosis health programme, rely heavily on public industries to supply their demands for medicines (see table 10) (Bastos 2006; Gomes et al. 2008). It is then argued that, because historically Brazil has been using non-bioequivalent medicines, it can provide important evidence for pharmaceutical regulation. Additionally, public producers argue that their medicines are not only safe but can also be therapeutically better. For instance, the antiretroviral didanosine (ddI) is emblematic, as Farmanguinhos discovered a formulation that was more effective than the one produced by the innovator firm, Bristol Myers Squibb. Although the product was not bioequivalent to the BMS original version, its bioavailability was substantially better (cf. Cassier and Correa 2003: 97).

**Table 10. Ministry of Health expenditure (US\$) on ARV purchases per pharma. Supplier. Brazil, 1996-2006.**

Laboratory	1996-2006	%
State level public laboratories	372,641,996	14.26
Federal level public laboratories	289,175,408	11.06
National private public laboratories	131,374,039	5.03
International private laboratories	1,820,614,256	69.65
Total	2,613,805,699	100.00

Source: Ministry of Health/National STD and AIDS Programme

How have public producers expressed these concerns in terms of policy preferences and demands? Interestingly, there are no records of public pharmaceutical producers' demands to reformulate or override the generic drug regulatory framework. Actually, there have been several discussions on how to get round the institutional constraints and adjust pharmaceutical products to the bioequivalence tests. There are three examples of this. Firstly, in July 2003 a seminar sponsored by the National Association of Public Laboratories (Alfob) together with the Minister of Health aimed to provide information about the situation of public pharmaceutical industries in Brazil (ANVISA 2003a; Oliveira et al. 2006). Although this would be a key opportunity to demand a revision or voice their dissatisfaction with the current regulation, participants suggested that one of the key areas for investment should be the restructuring of the system of quality, acquisition and equipments to conduct bioequivalence and therapeutically equivalence studies (Oliveira et al. 2006: 2386).

Secondly, an innovative strategy to adjust public industries to ANVISA's requirement was done in 2007 with the production of Efavirenz. That year, Brazil issued a compulsory license (CL) of Merck's antiretroviral Stocrin (details of this event will be discussed later on in this chapter) (Carta Capital 2007; Exame 2008; Agencia Brasil 2009). Although Brazil has been threatening to issue a CL of antiretroviral medicines on the grounds that they could produce cheaper versions locally, it was not able to promptly replicate Efavirenz in 2007 and the government had to import its generic version from India. It was only in 2009 that a public and private partnership between Farmanguinhos and three local private firms were able to deliver Efavirenz (Correio Braziliense 2009; Revista de Manguinhos 2009). This case was emblematic as it was the first generic drug produced by a public

pharmaceutical factory (and still so far). While the three private firms were responsible for synthesising raw materials, Farmanguinhos was responsible for the final formulation process (Revista de Manguinhos).

Thirdly, in 2009 the Sao Paulo state pharmaceutical industry together with the largest public pharmaceutical manufacturer in Brazil, Popular Pharmaceutical Drug Foundation (FURP) (Fundação para o Remédio Popular), inaugurated a new production unit in Americo Brasiliense to produce generic drugs for the treatment of chronic disease (Folha de Sao Paulo 2009; FURP 2010a). FURP has a particular role in supplying medicines to the state of Sao Paulo pharmaceutical assistance programmes (75% of its production) (Oliva 2007). In 2006, its production reached 2.5 billion pharmaceutical units and three thousand municipalities (FURP 2010). A particularly important client of FURP is the "Dose Certa" programme, a Sao Paulo state pharmaceutical assistance programme that has supplied essential medicines since 1995. The state of Sao Paulo invested nearly US\$ 90 million (R\$ 190 milhoes) to build the Americo Brasiliense unit and, during Jose Serra's administration as governor of Sao Paulo state (2007-2011), an additional US\$ 25 million (R\$ 50 milhoes) was invested in its pre-installation (FURP 2010a). The Americo Brasiliense unit will be managed through a public and private partnership (PPP), with the private sector responsible for the supply of APIs to facilitate generic drug production (Jornal O Imparcial 2009).

Finally, it is important to point out that the Ministry of Health has undertaken significant reformulations in its public laboratories. Besides the aforementioned challenges, public producers also face two structural market changes. Firstly, in 2006 a Ministerial Directive (*Portaria Ministerial 698/2006*) decentralised to sub-national states the responsibility for the public purchase of essential medicines. This severely affected the role of public industries, which would need to compete in a pulverised pharmaceutical market<sup>60</sup> (cf. Valor Economico 2009d; Costa 2010). For instance, the public industry Lafep reduced its annual revenue from R\$ 100 million in 2006 to R\$

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<sup>60</sup> Previous purchase of essential medicines was centralised at the Ministry of Health. Purchase of medicines from public producers does not require public auctions, thus guaranteeing a fixed demand for medicines produced in public industries.

70 million in 2008 (Valor Economico 2009d). Secondly, although reverse engineering capacity represented a technological gain, public laboratories still face a technological lag. The case of antiretroviral production is suggestive as AIDS patients live longer and demand more sophisticated medicines to control viral load resistance, for example. There is an increasing concern about the capacity of public producers in replicating complex medicines such as protease inhibitors (Lago and Costa 2009; Costa 2010).

In 2007, the Minister of Health, Jose Gomes Temporao, decided to reformulate the role of public pharmaceutical industries as part of the *Mais Saude* (More Health) programme, which refers to the Health Industry Complex. The intention is to increase the market regulatory role of these industries (Acesso Brasil 2008; Ministerio da Saude 2009a). In 2008, three ministerial directives initiated the process: (1) an inter-ministerial directive 128/2008 established that the public purchase of APIs should give priority to local private producers to stimulate national industrial development; (2) the ministerial directive 978/2008 listed several pharmaceutical products that are strategic for the Unified Health System (SUS), which refer to higher added-value pharmaceutical products usually, for example, in AIDS and cancer treatment; (3) while the ministerial directive 374/2008 created the National Program to Sponsor Public production and innovation in the Health Industry Complex. So far, the Ministry of Health has formed nine new public-private partnerships (PPPs) between seven state laboratories and 10 private companies to produce 24 medicines, which will be available through the National Health System (see annex 5) (Ministerio da Saude 2009a). It is still too early to assess the results and effects of this initiative. In 2009, during field research for this project, the Ministry of Health was still defining the business model for these public and private partnerships.

In sum, the fact that public pharmaceutical factories have been supplying the governmental pharmaceutical assistance programmes for decades with medicines that are not bioequivalent to an innovator product might raise doubts on the relevance of this requirement. It is not possible to say precisely what the effects or side effects

are of these products to the population's health, as it was not identified in any study monitoring this. Also, it was not possible to say precisely the exact number of medicines produced by these public factories that would be the subject of bioequivalence requirement (note that not all off-patent medicines are required to produce this certificate, only highly toxic drugs). Nevertheless, what is particularly interesting is the fact that many academic publications have mentioned the discomfort and concern of the public producers with this aspect of the generic drug regulation but little has been done in terms of advocacy to voice their disagreement. By contrast, it was possible to observe an adjustment of these public producers to the new institutional setting as they manoeuvre their limitations to adapt to this regulation (such as the bidding legislation of public procurement discussed in this section). Although public pharmaceutical producers have been less active in voicing their concern to some aspects of the generic drug regulation, AIDS activists has been upfront about this.

### **HIV/AIDS Activists**

Brazil is renowned for its vibrant HIV/AIDS activism and the engagement of disease-patients in the HIV/AIDS policymaking process (Galvao 2002a; Nunn 2008). Chapter four has demonstrated that, during the 1990s, AIDS activists centred their agenda on demanding the provision of medicines by pressuring the government through the courts and media (cf. Scheffer et al. 2005; Nunn 2008). Following this period of initial confrontation, AIDS activists became an important partner of the Ministry of Health in designing public policies and implementing prevention initiatives to a vulnerable population (Galvao 2000; Nunn 2008; Galvao et al. 2011). Finally, during field research for this study, it was possible to observe that AIDS activism in Brazil has evolved once again. This patient advocacy group has participated actively in pharmaceutical regulatory debates, not just pressuring government through media or protests but by closely informing decision makers about highly technical regulatory aspects. This section analyses this new capability of AIDS activism, how this came about and its implications to the generic drug regulation. More abstractly, this provides important lessons on the evolution of

interest group preferences by demonstrating how the content of AIDS activism has changed over time; however, it also contributes to understanding the structure of interest group representation in the pharmaceutical sector in Brazil. The latter refers to the fact that, as much as pharmaceutical firms have collaborated with government in the design of the regulatory rules for the sector, AIDS activists have also actively participated in these debates.

Some background information about the context of AIDS policy in Brazil in the 2000s is important in order to understand the demands of AIDS advocacy groups. Brazil was the first developing country to provide universal access to AIDS treatment for all those in need in 1996 and has provided important evidence to the global response to the epidemic since then (Nunn 2007; Nunn et al. 2009). The impact and relevance of the Brazilian response is assessed through its impressive health outcomes. Several studies have demonstrated a reduction of HIV/AIDS mother-to-child transmission, a decline in mortality, morbidity and HIV/AIDS related hospitalisation, and an increase in life expectancy and quality of life for people living with HIV/AIDS (Esau et al. 2003; Marins et al. 2003; Hacker et al. 2004; Teixeira et al. 2004; Campos et al. 2005; Matida et al. 2005; Dourado et al. 2006). The combination of prevention and treatment allied with government strategies to reduce the cost of medicines, such as price negotiations and local production of off-patent antiretroviral drugs, has been widely celebrated as the Brazilian model for AIDS treatment (Berkman et al. 2005; Cohen and Lybecker 2005; Greco and Simao 2007).

Although AIDS incidences in Brazil have been stable, the number of patients receiving treatment continues to increase. Patients receiving highly active antiretroviral therapy (HAART) have increased steadily, with an estimate of 200,000 patients in treatment in 2010 (Comissão Nacional de DST/Aids e Hepatites Virais 2010). Given that AIDS patients are living longer and with better quality of life, they will require more complex treatment (e.g. due to resistant viral strains). As antiretroviral drugs off-patent become clinically outdated, newer patent medicines are required (Nunn et al. 2007). For example, since 2008 Brazil incorporated three

new patent medicines to the therapeutic guidelines (Darunavir, Raltegravir and Etravirina). Brazil's expenditure on AIDS care and treatment had reached US\$ 201 million in 2007 (83% of total expenditure), raising much debate about the economic viability of the Program (cf. Granjeiro et al. 2007) and the concern of AIDS patient advocacy groups.

In 2001, by occasion of the debates on the Doha Development Round and the discussions on the TRIPS and Public Health declaration, the National AIDS Program began mobilising domestic activists on this matter. Records of the meeting of the Forum of AIDS non-governmental organisations of Sao Paulo state in October 2001 suggest this: "The forum was invited in an urgent meeting with the national coordination [of HIV/AIDS] to talk about TRIPS. There will be a meeting in Doha in November 9<sup>th</sup>, 2001 [...]" (Forum ONG/AIDS do Estado de Sao Paulo 2001: 1). The report continues to explain that AIDS activists were supposed to write a statement of support and mobilise other NGOs in Brazil and abroad, pressuring the WTO members to sign the TRIPS and Public Health declaration. The National AIDS Program requested that NGOs should enforce the statement: "Nothing in TRIPS agreement should limit its members from taking actions to protect public health" (Forum ONG/AIDS do Estado de Sao Paulo 2001: 1). In other words, the crisis in the pharmaceutical sector and the support of the Ministry of Health created an incentive for AIDS groups to organise an agenda on regulation of medicines that was absent until then.

One of the most active civil society advocacy groups in the pharmaceutical regulation is the network of NGOs in the Working Group of Intellectual Property (WGIP), created in 2001 by a joint initiative between the international non-governmental organisations Oxfam, Action Aid and several local NGOs, such as IBASE and GAPA. This group is hosted by the Brazilian Network for the Integration of the Peoples (Rebrip) and coordinated by the Brazilian Interdisciplinary AIDS Association (ABIA). Its members include organisations working with people living with HIV/AIDS, human rights and consumers' rights. Initially, the GTPI's primary concern was to consolidate different organisations and empower their political actions around intellectual property affairs (GTPI 2010). In 2003, an internal



decision by Rebrip tailored the group's focus on access to medicines and intellectual property affairs, which previously incorporated seeds and biodiversity issues as well (*ibid*).

Rebrip invited the Brazilian Interdisciplinary AIDS Association (ABIA) to coordinate the working group. ABIA is one of the foremost non-governmental organisations responsible for AIDS advocacy in Brazil, but also disseminates accessible information about the disease and provides health interventions (such as support groups) to people living with HIV/AIDS (PLWHA). The former coordinator of the GTPI, Carlos Passarelli, recalled that initially the core aim of the working group was to engage in traditional advocacy initiatives, such as to disseminate the implications of intellectual property affairs to public health and make this complex/technical topic more accessible for other Brazilian NGOs (Passarelli 2009). This was done by preparing seminars and workshops to empower leaderships in the issue (*ibid*). Passarelli also explained that during his tenure there was limited discussion about generic drug regulation and, although the issue of bioequivalence was raised once, the debate never evolved.

However, in mid-2000 the GTPI expanded its activities and has been assisting the Brazilian government (executive, legislative and judiciary) in the (re)design of pharmaceutical regulatory rules. It is difficult to pin down exactly when this participation in regulatory affairs began. Based on the extensive field research for this study, my interpretation is that this evolution of AIDS activism relates to the current generation of highly-skilled activists participating in these NGOs. For example, Renata Reis and Gabriela Chaves have been representing NGOs activists in several public discussions about pharmaceutical regulation. Reis is a lawyer with expertise in public health and political science, while Chaves is a pharmacist with expertise in Public Health. Both have worked in the Pharmaceutical Assistance Division of Fiocruz (NAF), which is well known for its engagement in national and international intellectual property and access to medicines studies and advocacy (cf. Bermudez et al. 2000). Renata Reis is the current coordinator of GTIP and Gabriela Chaves is currently responsible for the Access to Medicines division of Brazil's

*Medicine Sans Frontier* but has worked closely with ABIA in the past. With the expertise of those from different aspects of the pharmaceutical regulation, ABIA has been able to mobilise extensive support of other NGOs but has also collaborated more closely with the government in the regulatory process in this sector. This process has required constant learning on how to act in regulatory lobbying as the following two sections demonstrate.

### **Regulation of antiretroviral generic drugs**

Before discussing the position and demands of Brazilian AIDS activists on the generic drug regulatory rules in Brazil, it is important to situate the reader in relevant international events on this topic. This contextual information is particularly important, as their criticism resembles an increasing disagreement of international NGOs with the stringent rules adopted by developed governments and international agencies to regulate generic medicines. Besides, the Brazilian case could provide relevant evidence for this discussion, as we shall see.

The documentary evidence collected for this thesis suggests that contestation around bioequivalence tests and antiretroviral drugs began in 2003. The World Health Organization has a service to pre-qualify generic drugs and producers that intend to supply medicines to the United Nations procurement agencies (for example, UNICEF) or other organisations such as UNITAID, the Clinton Foundation and the Global Fund that provide medicines to developing countries. Once these producers are certified, they are allowed to compete in the procurement and supply of medicines to international agencies or countries. WHO sets its own standards to certify the quality and safety of medicines, including bioequivalence requirements (World Health Organization 2005; 2006). In August 2003, the Pre-Qualification Program decided to exclude from its certified list three antiretroviral drugs produced by Indian firms that had “been found non-compliant with international standards of good clinical and laboratory practices” (Hogerzeil 2004; World Health Organization 2004b). A few months later, other Indian firms temporarily withdrew their medicines from the list to carry out bioequivalence tests (Reuters 2004; World Health Organization 2004a). These decisions raised much debate among AIDS activists and

Pan-American Health Organization advisors as to whether bioequivalence is a pre-condition to define quality of medicines (Gonzalez and Rossi 2004).

Gonzalez and Rossi, advisors for the Pan American Health Organization, published a paper in *Boletín Farmacos* entitled “Bioequivalence, ambiguity, opportunism and the case of exclusion of antiretroviral drugs from the WHO Pre-qualification list” (Gonzalez and Rossi 2004). The authors severely criticised the WHO’s decision on the grounds that bioequivalence cannot be used as a parameter to assess quality of medicines and made an effort to clarify the place of bioequivalence in the manufacturing process. They also called attention to the fact that bioequivalence requirements can serve as technical entry barriers to limit competition in the pharmaceutical sector (Gonzalez and Rossi 2004: 6). Similarly, Gonzalez (2008) questioned the unproblematic use and the publicity of bioequivalence tests as a standard to assess quality of medicines. What these authors claim is that regulatory authorities should be careful when designing their frameworks, as stringent norms does not necessarily assess the quality of medicines; it can reduce market competition and ultimately harm access to medicines.

The Pan-American Health Organization (PAHO), through the Pan American Network for Drug Regulatory Harmonization, [http://new.paho.org/hq/index2.php?option=com\\_content&do\\_pdf=1&id=1054](http://new.paho.org/hq/index2.php?option=com_content&do_pdf=1&id=1054) has made efforts to harmonise the regulatory rules in Latin America, including Good Manufacturing Practices<sup>61</sup> and bioequivalence tests (cf. Pan American Health Organization 1997). In 2005, in an annual meeting organised by PAHO to discuss these issues, representatives of the Health Action International (HAI), an independent global network that promotes access and improve the rational use of essential medicines, defended the “elimination of a generalised demand for the use of bioequivalence for ARV products, and rather its use on a case-by-case basis” and “the importance of fulfilling good manufacturing practice as a determining factor in

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<sup>61</sup> Good Manufacturing Practice (GMP) is “part of quality assurance which ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorization. GMP is aimed primarily at diminishing the risks inherent in any pharmaceutical production, which may broadly be categorized in two groups: cross contamination/mix-ups and false labeling”.

the quality of drugs” (Health Action International 2006: 36). Brazil is usually quoted by those who contest the concept of bioequivalence as a country that has successfully used antiretroviral drugs without going through these tests to treat AIDS patients and is one of the most successful responses to the HIV/AIDS epidemic in the world (Gonzalez and Rossi 2004).

[http://new.paho.org/hq/index2.php?option=com\\_content&do\\_pdf=1&id=1054](http://new.paho.org/hq/index2.php?option=com_content&do_pdf=1&id=1054)

The first incursion of Brazilian AIDS activists in questioning sanitary regulatory rules was taken ambitiously by ABIA. A booklet published by ABIA in 2007, *Medicamentos: falando de qualidade* (Medicines: talking about quality), for the first time challenged the association of bioequivalent generic drugs with quality medicines (Ruiz and Osorio-de-Castro 2008). It explains that several steps in the manufacture process, such as Good Manufacturing Process, assure the quality of drugs and that bioequivalence should not be considered one of them. They argue that this misconception is diffused by those who want to make a profit out of it. Thus, bioequivalence is seen a technical barrier for access to medicines, as its requirement can reduce or delay market competition. “Without competition, there is a market monopoly [...] its result is enhancing profit of one manufacture or a selective and small group” (Ruiz and Osorio-de-Castro 2008: 48). To support these arguments, the authors mention the celebrated National AIDS Program:

This is exactly the case of antiretroviral drug produced in public laboratories in Brazil. As same as similar products, it is not therapeutically equivalent to an innovator drug. But these drugs work for patients, as we can see in more than 10 years that these medicines have been used in the country. During this period, universal treatment with similar drugs has completely changed the face of the [AIDS] epidemic in the country. It would be completely absurd to say these drugs do not have quality because national similar antiretrovirals are not bioequivalent to a innovator version (Ruiz and Osorio-de-Castro 2008: 45-46).

The motivation for this publication was initially to discuss the concept of “quality of medicines” because many AIDS activists were voicing that Brazilian pharmaceutical products were better quality than the ones produced in India and China, or that brand-name products were better than their generic version (Chaves 2009). Gabriela Chaves, responsible for organising this publication, explained: “The industry has done a perfect lobbying, such as that many activists are now using this discourse without even knowing what bioequivalence is”. Chaves is careful to emphasise that

bioequivalence is an important parameter, but one must assess medicines with a narrow therapeutically window (that is, small doses above or below the prescribed could be toxic)<sup>62</sup>. She points to the complexity of putting healthy individuals into clinical trials and the costly infrastructure required to provide these tests. “Is it so important to have curves exactly the same, comparing a reference product to a generic? Sometimes it happens to have bioavailability of a generic product better than a reference product”, she states. Thus, their advocacy agenda is to detach the discourse of bioequivalence from quality assessment, given that bioequivalence in itself is not a parameter to assess quality of medicine. Renata Reis, a lawyer and coordinator of the GTPI, corroborated this concern:

We [GTPI] have an advanced position related to this [interchangeable tests], we do not believe that bioequivalence and bioavailability is equal to quality, we don't believe in this. [...] We listened to the thesis of Division of Pharmaceutical Assistance (Fiocruz) that has a good study on this, feet on the ground, about quality of medicines. Our flagship, WGPI flagship, is quality and this is not the same as 'if you have bioequivalence and bioavailability this will be the best option' (Reis 2009).

This is also the position of Celia Chaves, a pharmacist with long experience in pharmacology tests and president of the Brazilian Federation of Pharmacists. She is aligned to ABIA and GTPI's position:

What doesn't make sense is to say that similar drugs must provide bioequivalence tests, because it will then be transformed into generic. In reality this is what the industry is pressing [...] transform all similar into generic. The fact that similar drugs do not have bioequivalence doesn't mean it is not good; the only difference is that it is not bioequivalent. In other words, I simply can't do the same treatment [protocol] with similar drugs, the same treatment I was getting with an original drug, or reference or generic [...]. Maybe I will need to use a prescription a little bit different, this doesn't mean it is not good (Chaves 2009).

The discourse of these activists raises several concerns. Firstly, increasing the stringency of generic drug regulation by mandating off-patent drugs to be an equal copy of an innovator product will not necessarily increase the quality of medicines. In fact, it could reduce the supply of medicines and reduce competition. Market competition in this context is crucial for reducing the price of medicines and

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<sup>62</sup> Gabriela Chaves coordinates the Access to Medicines campaign of Doctors Without Borders (DWB) in Brazil, but her opinions do not express the NGO's position on this matter. She agreed to be interviewed for this study and clearly stated that she speaks as a pharmacist and not for the DWB.

increasing access to affordable medicines. A second concern is that it reduces the potential of national industry, as Brazil has a significant number of private pharmaceutical industries and the whole public pharmaceutical industry will be severely harmed by 2014, when the grace period to adjust their products expires. Thirdly, it gives a false impression that medicines produced in Brazil are less effective than those that are bioequivalent and produced in India, for example.

How are these concerns expressed in terms of policy demands? What has been done to reverse or adjust the policy path? Interestingly, besides the aforementioned publication there was no record of advocacy or lobbying demands to reformulate the generic drug regulation. Chaves explains that much of the discourse of bioequivalence associated with quality was incorporated into the discourse of experts and activists to an extent that it is difficult to question. The fact that WHO requires these tests further legitimises and reinforces the matter. Thus, it is important to point out that this is not the mainstream speech of AIDS activists; while some activists are not concerned with pharmaceutical regulation at all, others agree that generic medicines must equal their innovator versions. The intention of the booklet on quality of medicines was to make this topic accessible and place it on the activism agenda, the authors argued. The acceptance of the idea that off-patent medicines must equal their innovator versions, and the difficulty in mobilising the bulk of AIDS activists against it, suggests that the regulatory concept of bioequivalence has been incorporated by these patients to an extent that might become difficult to reverse. Mostly important, we can observe, by comparing the antecedent period of the reform with the narrative of this section, how these activists that were not participating whatsoever in pharmaceutical regulation have slowly become aware of the implications of this rule. Thus, this also exemplifies how a narrow deduction of their interest, as proposed by rational choice scholars, would ignore this important element of the regulatory process of generic drugs in Brazil.

During field research for this project, it was possible to observe that some of the local pharmaceutical producers who did not adapt to the generic drug reform have had similar criticisms as the AIDS activists to the bioequivalence requirements.

However, when questioned about a possible collaboration with these industrialists, some of the NGO interviewees confirmed the little contact between them and mentioned a relatively recent contact with Abifina and GTPI in an ongoing project on intellectual property issues (discussed below). I was given two reasons for this limited alliance. Firstly, one interview explained the infant participation of NGOs in the regulatory negotiations and limited experience in regulatory advocacy practices (Interview with patient advocacy informant A 2010). Secondly, another interviewee mentioned that this could be associated with the “nature” of their interests (Interview with patient advocacy informant B 2009). While private firms are concerned with profit, activists are worried solely about public and public health interest.

To sum up what has been discussed in this section, despite these initial attempts to bring the issue to the agenda and voice their concerns with some aspects of the generic drug regulation in Brazil, this subject has not received much attention. Some interviewees expressed concern in bringing this topic to their advocacy agenda, as apparently there is a consensus among segments of their group that off-patent medicines should be equal to an innovator drug otherwise will not be as effective (Interview with patient advocacy informant A 2010). Furthermore, the support of the World Health Organization to the bioequivalence tests with the Pre-Qualification Programme and through their guidelines further legitimise this norm (cf. World Health Organization 2001; Embrey et al. 2009), making it difficult to convince their peers of the importance of debating this topic. Furthermore, the agenda of AIDS activism has particularly concentrated on monitoring intellectual property affairs. This is discussed in the next section, along with the consequences for the generic drug policy path.

### **Multiple interests: the intellectual property debate**

The GTPI has been the most active group within civil society in voicing their opinions against intellectual property issues. During field research for this project, I also met representatives of diabetes patients. However, interviewees mentioned that

only recently had they learned about how intellectual property issues can affect access to medicines, thus they were less able to comment on the events happening in this field.

This section discusses several important actions taken by the GTPI to contribute to the IP debate in Brazil. Similarly to chapter 5, the analytical exercise here is to assess how their intellectual property agenda affects their lobbying activity in generic drugs, but also the path of this regulation, assuming that actors might have multiple interests as discussed in chapter 2. For comparative purposes, this section is divided into the three intellectual property issues as presented in the previous chapter. However, there are other areas where AIDS activists are participating (such as compulsory license), which are introduced as a fourth item.

### **Pipeline mechanism**

AIDS activists began to participate in the debate on pipeline mechanism in mid-2000s. A revision of newspaper articles published in the 2000s evidenced that they began voicing their concerns over this issue in 2006 (cf. Reis and Chaves 2006). Their concern is that, among the 1,182 pipeline patents requested by innovator pharmaceutical firms, four are antiretroviral drugs and 18 have been on the list of exceptional medicines provided by the Unified Health System (Jurberg 2008; Terto Jr et al. 2009). For example, Efavirenz is an antiretroviral drug used by 87,000 of the 190,000 patients being treated for HIV/AIDS in Brazil and was protected by a pipeline patent (Terto Jr et al. 2009). In 2007, the GTPI organised a seminar to discuss the pipeline mechanism. As a result of this event, the group decided to directly interfere in the problem (Interview with patient advocacy informant B 2009).

Similarly to Pro-Genericos, which has gone through the courts to avoid patent extensions, AIDS activists have also been participating as *amicus curia* in several law suits. For instance, in November 2007 the GTIP presented to the Brazilian Prosecutor a petition claiming the unconstitutionality of articles in the Patent Act that refers to pipeline mechanism. It requested that the prosecutor file a Direct Action of Unconstitutionality (ADI) with the Supreme Court (given that civil society cannot fill



the procedure by itself) (Reis et al. 2009). ADI is a judicial instrument that allows federal authorities to revise the constitutionality of the law or normative act. If their request is accepted by the Supreme Court, the legislation on pipeline mechanism can be removed from the legal system. GTPI claims that pipeline mechanism is unconstitutional for four reasons: 1) pipeline patents granted in Brazil were already in the public domain, which contradicts the principle of absolute novelty for patents; 2) it violates the principle of reasonability and proportionality, as its patent is granted without the analysis of material requirements (the INPI does not assess these application, as a patent is approved based on international patent office reports); 3) it violates the principle of equality as it differentiates between national and foreign products. While national industries have to go through the INPI, foreign applications are submitted only to their originating countries (whose requirements can be different from Brazil); and 4) it violates social interests as it allows a monopoly of knowledge that was already in the public domain, unnecessarily increasing the expenses on medications (for government and patient budgets) (Terto Jr et al. 2009: 16-17).

In 2008, the GTIP's demand received the support of the Ministry of Health. The Director of the Department of Pharmaceutical Assistance, Dirceu Barbano, declared in a newspaper interview: "From the point of view of the MoH, the Pipeline brings prejudice to the development of the country and has a series of impacts on the Brazilian public health" (Estado de Sao Paulo 2008b). Barbano cited the example of a cancer medicine, Gleevec, the costs of which could be reduced by 90% if there was no pipeline patent. Its costs are estimated at US\$ 5,000 per patient/month.

In May 2008, the Brazilian Prosecutor General sent the case to the Federal Supreme Court questioning the constitutionality of the pipeline mechanism on the grounds that it does not respect the principle of novelty, for those patents were already under public domain when granted. If accepted by the Supreme Court it could invalidate the patent of 565 medicines protected under this rule. Until October 2009, 11 pharmaceutical associations (Pro-Genericos, Abifina) and NGOs had filed requests to participate as *amicus curia* in the litigation, but only Interfarma (which represents the interests of research-based firms) was accepted (Valor Economico 2009a). Note

that the initial movement to issue the ADIN was taken by the NGOs, not the business association. However, as soon as the Prosecutor sent the case to the Supreme Court, several local producer representatives joined and supported the strategy (Valor Economico 2009a; 2009b; 2009c).

Note how the agenda of activists resembles the preferences of Pro-Genericos presented in the previous chapter. These activists have also used similar strategies to inform the government about the pipeline mechanism and its impact on the production of generic medicines (e.g. amicus curia). On the other hand, activists have taken a leadership role in mobilising the Brazilian General Prosecutor to question the constitutionality of the pipeline mechanism, a movement that has then been followed by other business associations by filling requests to participate as informants of the Supreme Court.

#### **TRIPS Plus agenda: polymorphs and second use**

In 2007, the representatives of GPTI became aware that the INPI was revising its patent standards through the newspapers. As we have seen in the previous chapter, INPI invited representatives of the pharmaceutical sector and ANVISA to discuss a possibility for reformulating Brazil's patent standards. Renata Reis requested the institute to allow her to participate in these discussions as a member of civil society: "they said I couldn't go because it was a meeting for pharmacists, doctors and that was a technical meeting not a political one. [...] Then I said I was gonna send my pharmacist. Gabriela was working with me". She continues: "Once she got there, there were many industry lawyers. So we understood that it was a resistance for [talking to] some lawyers, not all lawyers. And they justified this by saying that those lawyers that were there were both chemists and lawyers" (Reis 2009). AIDS activists voiced that these meetings had been held in closed sessions, thus excluding the participation of civil society on the grounds that it should only include experts.

During a public hearing in Congress, the Federal Deputy Paulo Teixeira questioned the president of INPI, Jorge Avila, to clarify the exclusion of chronic disease patient representatives of these meetings (Camara dos Deputados 2007a: 56-57). The INPI argued that this was due to their inexperience in conducting public consultations and

apologised for their clumsy behaviour (Avila in Camara dos Deputados 2007a: 61). While the INPI claim that this is a strictly technical matter, HIV/AIDS activists highlight the political component of this decision: “The interpretation of patentability standards is not a technical issue, but a political decision, especially in the pharmaceutical field” (Reis et al. 2009: 41). The relevance of this event is two-fold. First, it shows the importance of AIDS activists, who called attention to the politics of the patent application process which, so far, had been seen as a methodological decision ignoring the different interests in this issue. Second, it also demonstrates how these activists are claiming their rights to inform the government on topics sensitive to public health, rather than just pressure for access to medicines. The initial resistance of INPI to allowing their participation in technical meetings shows how these activists were seen as less able to contribute in the debate, thus they had to claim their right (and also demonstrate capacity) to collaborate in this discussions.

Looking at the AIDS activists’ preferences and demands, it is possible to see similar demands as the ones defended by local industrialists. They also support the fact that second medical use and polymorphs should not be granted patent protection. The former is due to its lack of novelty, given that what would be protected by a patent is the medical therapeutic indication, not the product. This also implies a lack of industrial applicability, as a patent of “second medical use” would protect the effects of the substance on the body (not the method of manufacture). The objection to patent a polymorph is that polymorphism is a natural property (discovered in ordinary experimentation) thus cannot be considered a human invention (Reis et al. 2009: 39-41).

Particularly interesting is how the AIDS activists have voiced their demands. They have monitored and participated in virtually every governmental discussion on this topic. Besides actively participating in the INPI’s meetings on the revisions of the patent standards, the GTPI has also been participating in legislative activities (Reis et al. 2009). Regarding the Bill Law 2511/2007 that proposes to eliminate the patent of second medical use and polymorphs, the group wrote a complementary legal opinion, supporting its approval and quoting other countries that have taken similar decisions

(such as India and Argentina). Additionally, the group has educated Congressmen on the international guidelines provided by WHO, which do not recommend patent protection for second use and polymorphs (Reis et al. 2009). During the public hearings of this project in Congress, the activist Michel Lotrowska from Doctors Without Borders (member of GTPI) was invited to present its arguments together with representatives of the government and pharmaceutical industries (Camata 2008). This highlights now only how these activists have gained space and legitimacy to voice their demands on technical aspects of pharmaceutical regulation, but also how these preferences and demands are similar to the generic drug manufactures.

### **Procedure to register pharmaceutical patents in Brazil**

Regarding the discussions on the prior consent mechanism, such as Pro-Genericos, the GTPI has petitioned in favour of this institutional arrangement. In November 2009, the GTPI was invited, together with other representatives of research-based pharmaceutical industries, for a public hearing in Congress to debate the Bill Law 3709/2008 (which discussed the role of prior consent). The GTPI, represented by Celia Chaves, president of the Brazilian Federation of Pharmacists, strongly supported that prior consent should remain unaltered. It supported the idea that this institutional arrangement was important in order to keep patent examination standards high and thus avoid underserved patents (Chaves 2009). Furthermore, they argued that this arrangement is aligned with the TRIPS and Public Health (Doha Declaration) that states public health should override commercial interests, and with the 2008 WHO Global Strategy on Public Health, Innovation and Intellectual Property (WHA 61.21) that states countries should always consider adapting their national legislations to fully use TRIPS flexibilities (Chaves 2009). This position was also aligned with ANVISA's perspective on this issue and Pro-Genericos, which were also participating in this public hearing.

### **Additional agendas**

As seen so far, the agenda of AIDS activism and local producers has synchronised with respect to pipeline patent, patentability standards and rules of patent examination. Furthermore, both actors have presented their claims in similar forums

and used similar strategies. However, AIDS activists have gone a step further. While Pro-Genericos and other representatives of national industries have been silent about the Brazilian government negotiation with multinational pharmaceutical firms over the price of antiretroviral drugs, AIDS activists have vehemently supported the use of TRIPS safeguards. For instance, the president of Pro-Genericos, Odimir Finotti, has constantly suggested that it is not the Association's intention to challenge patent rights or propose amendments in the Patent Act (cf. 2009a; 2009b). This subsection describes two additional events in which the NGOs collaborated with government in cases of intellectual property debates that could impact on the market for off-patent antiretroviral drugs: the Tenofovir pre-grant patent requirement and the Efavirenz compulsory license. For clarity purposes, I will provide a brief description of each case and the role of AIDS activists in each of these and how these relate to the generic drug regulation.

#### (1) Tenofovir and Kaletra pre-grant opposition

In December 2006, seven NGO members of the GTPI (ABIA, Conectas, Grupo Pela Vidda/ SP, GAP/SP, GAP/RS, Gestos e GIV) filed a request with the INPI opposing the patent application of two antiretroviral drugs, a second patent application for Kaletra (Abbott), and a patent application of Gilead's Viread (Tenofovir Disoproxil Fumarate). Pre-grant opposition is an administrative mechanism of the Patent Act (article 31) that allows any interested parties to provide documents and information to assist patent examination. Thus, the intention was to clarify why the INPI should not grant these two patent applications.

The arguments opposing these patents were distinct. The case of Tenofovir Disoproxil Fumarate refers to the fact that Gilead's requested a patent of an active ingredient that is used to treat HIV infections (Request N° PI9811045-4). However, AIDS activists argued that the only active ingredient that acts on the virus is Tenofovir, while the Disoproxil assists in fostering the availability of Tenofovir to react with the virus, while Fumarate provides better stability for the medicines (Abia 2006: 9). Both Tenofovir and Disoproxil had their patents expired 15 and 9 years prior to this new grant application. The activists also argued that the use of Fumarate

salt is a chemical practice known since 1963. Together, these arguments reinforced the fact that Gilead's application did not fulfil the patentability requirements of the Brazilian legislation (article 8 of the Patent Act). In 2008, the Ministry of Health declared Tenofovir of public interest, which sped up the application revision by the INPI (Ministerio da Saude 2008; Estado de Sao Paulo 2008a). Gilead's request was denied in April 2008 (INPI 2008) and its appeal denied in July 2010 (INPI 2010a), on similar grounds argued by the GTPI. The case of Kaletra refers to the fact that Abbott requested a second patent of this medication (divisional patent application, which split the uses of a single invention into separate patents) (Request N° PI1101190-4). The first patent was granted as a pipeline mechanism and AIDS activists argue that, according to the Patent Act, there is no legal provision for divisional applications under the pipeline mechanism, thus the INPI should deny the patent request (Abia 2006; Chaves et al. 2008; Reis et al. 2009).

Particularly interesting in these two cases is the capacity of these NGOs to provide information and support a decision that is highly technical, collaborating with the INPI in the process of patent approval rather than just using pressure or media fanfare to express their criticism.

## (2) Efavirenz compulsory license

Efavirenz is a protease inhibitor, commercialised in Brazil by Merck under the brand-name Stocrin and was used by nearly half of AIDS patients in need of treatment in 2007 (Nunn et al. 2007). Similarly to Abbott, Merck also has a long tradition of negotiating price with the Brazilian government, reducing its price by more than 50% since 2001 (Ford et al. 2007; Nunn et al. 2007). However, as both Kaletra and Stocrin became a convenient treatment choice (e.g. fewer pills), more patients were put into treatment in 2003 and 2004. A scale-up of treatment with these drugs offset the price reductions offered until them (Nunn et al. 2007). Furthermore, the price of both drugs in Brazil was lower than the price for other middle-income countries with similar HIV prevalence rates, but significantly higher than the average price of its available generic drug version (*ibid*). Brazil demanded a price reduction of Efavirenz from US\$ 1.59/daily dose to US\$ 0.65/daily dose, based on the

following two arguments. Firstly, other countries such as Thailand were paying a much lower price for Efavirenz than Brazil and, secondly, there were generic drug versions of Efavirenz produced by Indian companies at a much lower price (Simao 2009).

Facing an increase in the number of patients under treatment, thus also an increase in the expenditure on antiretroviral drugs, the government had three alternatives: (i) reduce the scope of the programme, thus limiting the number of patients; (ii) substantially increase the allocation of resources for AIDS treatment; or (iii) override patent protection and reduce the cost of Efavirenz, thus facing possible economic retaliations. However, since Brazil has a Federal Law mandating the government to provide antiretroviral drugs to all patients in need, reducing the scope of the programme would allow AIDS patients to file law suits against the government in the event of stock running out (cf. Scheffer et al. 2005). Similarly, an increase in the allocation of resources into AIDS treatment would be less possible given that the high cost of the programme had threatened its financial sustainability (Granjeiro et al. 2007). Thus, the third option was the most viable. Although Brazil has a long tradition in threatening to use a compulsory license and locally producing medicines to induce pharmaceutical companies into reducing their prices, this strategy was becoming less efficient as time went by (cf. Ford et al. 2007; Nunn et al. 2007).

After several meetings with Merck, the Minister of Health, Jose Gomes Temporao, decided to declare Efavirenz of public interest (the first step to issuing a compulsory license) in April 2007 (Ministerio da Saude 2007a). On 4 April 2007, Merck offered a price reduction of US\$ 1.10 and committed to transfer Efavirenz technology to Brazil by 2010 (two years before its patent expired). Furthermore, Merck counter argued that its price tier was established together with the World Bank, World Health Organization and other United Nations agencies according to the country's Human Development Index (HDI) and the prevalence of HIV/AIDS (Boletim da ABPI 2007). While Brazil and Thailand have a similar HDI, the prevalence of HIV/AIDS in Thailand is three times higher than Brazil (less than 1%) which, arguably, would not justify similar prices (Boletim da ABPI 2007). Ignoring this claims, the Minister

of Health Jose Gomes Temporao and President Lula signed a Decree declaring that Efavirenz was of public interest and issued its compulsory license (Brasil 2007). The compulsory license for public interest refers to the fact that Brazil could locally produce these drugs for non-commercial purposes but would still pay 1.5% in royalties for its use (Valor Economico 2007b). In his speech, President Lula ratified the compulsory license:

It doesn't matter if the firm is German, Brazilian, French or Argentinean. The concrete fact is that Brazil cannot be treated as a country that does not deserve respect. That is, we paid US\$ 1.60 while the same medicine is sold to another country at US\$ 0.60. This is rough, not just from an ethical perspective but from a political and economic point of view. It is disrespectful. It's like the Brazilian patient is inferior to a patient in Malaysia (President Luis Inacio Lula da Silva in Agencia Brasil 2007).

The NGOs supported the government at every step of this negotiation (GIV. 2007; GTPI 2007; GTPI 2007a). The National AIDS Program informally consulted the AIDS activists during the process. In this meeting, several alternatives were discussed in order to issue a compulsory license according to the Brazilian legislation, looking at the possibilities and constraints of each one and the perspective of civil society (Interview with government official D 2009). The relevance of Efavirenz's compulsory license is twofold. First, it further demonstrates the participation of NGOs in intellectual property discussion and their role in supporting the government's decision with technical information and legitimising this decision. Second, it illustrates the fact that their advocacy evolved beyond demands for access to medicines in order to monitor the regulatory bottlenecks that could limit the availability of medicines.

The case of compulsory licence of the antiretroviral Efavirenz also adds another important element to the analysis of this chapter. After overriding the patent for Efavirenz in 2007, the government had to import its generic version from India. This is particularly surprisingly, as Brazil has threatened to issue a compulsory license for Efavirenz since 2001, arguing that it had the capacity to produce this medicine at a lower price in the public pharmaceutical industries (Ford et al. 2007). The fact that both Farmanguinhos and Lafep were able to deliver the first batch immediately after



the compulsory license raised much debate about the capacity of public industries to effectively produce medicines that require complex technological capacity.

The Director of Farmanguinhos, Eduardo Costa, explained that initially Lafepe presented studies informing of its capacity to produce this medicine; however, it failed to pass in the bioequivalence tests later on (Costa 2009). Note how the bioequivalence norm once again affected the production capacity of these firms. Brazil imported a generic drug version of Efavirenz from an Indian company for two years following the compulsory license. It was only in 2009 that Farmanguinhos, in collaboration with three local private laboratories, launched its first batch of the bioequivalent Efavirenz. This was the first generic medicine produced by a public pharmaceutical industry (Revista de Manguinhos 2009). However, the price of the Brazilian generic version of Efavirenz is higher than the one imported from India (US\$ 0.46/per dose), but still lower than the price offered by Merck (US\$ 0.59 against US\$ 1.56/per dose).

Naturally, this raises the question of the extent in which production of medicines in public firms is relevant to improving access to medicines in Brazil, particularly given that other studies have already highlighted that the prices of these drugs are much higher than international ones (cf. Nunn et al. 2007). Additionally, while prices of generic drugs are declining elsewhere, they are increasing in Brazil (*ibid*). Arguments of the relevance of public production of medicines are debatable and were already presented earlier on in this chapter. What is relevant here is the position of AIDS activists in this debate as it demonstrates that, although they have a similar agenda to the drug manufactures, there is no evidence of collusion between them:

AIDS activists in Brazil recognize that public production of medicines is not perfect but see clear advantages in the Brazilian model. For these activists, the objective is access to quality medicine from any supplier. Whilst private drug companies do provide quality medicines, they are not transparent in detailing the costs of production or how they set prices. Activists understand that the high cost of new treatments threatens the sustainability of Brazil's universal treatment programme; obtaining strategic information from public labs is therefore crucial to their advocacy efforts (Flynn 2008: 530).

Following Flynn's assertion, the documentary research for this thesis also found that the position of AIDS activists regarding public production of medicines is that they acknowledge the place of public production, but clarify that their core agenda is the access to medicines campaign (Reis et al. 2009: 28; Vieira and Reis 2009). They support that the combination of imports, followed by local production, is essential to assuring the success of Efavirenz's compulsory license; thus hoping that, with an increase in the scale of production and manufacturing experience, public pharmaceutical firms will be able to reduce these production costs (Reis et al. 2009: 28; Vieira and Reis 2009).

## **Conclusion**

This chapter explored the unexpected effects of the generic drug regulation and the reaction of actors that had not been engaged in this debate to date. It shows how the regulation affects the production of medicines in public pharmaceutical factories and why they are unable to fulfil the bioequivalence requirement. Despite the disagreement with this component of the regulatory norm and the fact that they have been supplying governmental programmes for decades with products that were not bioequivalent, public producers decided not to publicly voice their concerns and made efforts to adapt to the regulatory context. In this sense, AIDS activists have become aware of this drawback in the production of antiretroviral medicines in public factories, which leads to an important finding of this chapter.

This analysis of the participation of AIDS activists in the regulatory process has provided important evidence on how lobbying activity is a learning practice and how preferences are constructed within the policy process. It demonstrated that, although AIDS activists were less aware of the pharmaceutical regulatory process and its influence in their stakes during the 1990s, in the course of the 2000s their preferences were adjusted. AIDS activists became familiar and highly active in different aspects of pharmaceutical regulation, ranging from generic drugs to intellectual property affairs. They have also successfully mobilised other groups of civil society into these issues through the Working Group of Intellectual Property (GTPI). Thus, it could be

argued that the HIV/AIDS activism in Brazil has evolved from pressuring government for the provision of public goods and partners in the design and implementation of the Brazilian response to the epidemic in the 1990s (cf. Galvao et al. 2011), to a collaboration in the pharmaceutical regulatory process in the 2000s. As for the content of their policy preferences, they have questioned the slogan of “high quality medicines” attached to the generic drug products and the concept that off-patent medicines must be equal to its innovator version. However, this agenda has been offset for several reasons. One is the difficulty to go against the appealing slogan of “high quality products” as this has been diffused and accepted by the other activists and society in general. Second, they have placed more weight on the intellectual property agenda, which offset the advocacy agenda on the generic drug regulatory process. This shows that, although there are concerns over the path of the regulatory process of generic drugs in Brazil, little has been done to change or adjust this policy path or even educate decision makers about them.

The analysis of the political demands of these activists also resembles the theoretical concepts discussed in chapter 2 on the structure of interest representation in the pharmaceutical sector in Brazil. This chapter has demonstrated that, similar to business representatives, activists have collaborated with the government in different intellectual property affairs. Comparing both, it is possible to observe that much of the advocacy agenda of these activists synchronise with the demands of Pro-Genericos and local pharmaceutical producers in general. Both are concerned with the development of the pipeline mechanism, the revision of the intellectual property resolutions by the INPI and also the prior approval institutional arrangement for patent application. However, activists have gone a step further and advocated for compulsory license and obstructed the patent request of some antiretroviral drugs. Furthermore, both actors (business and NGOs) voice their claims in similar forums and use similar strategies (such as filling *amicus curia* to assist court decisions), but it was not possible to observe any form of collusion between them. It is also noteworthy that, by positioning themselves with similar policy demands as business representatives, AIDS activists also legitimise the claims of generic drug manufactures. Thus it could be said that the aggregate effect of these two phenomena

-- legitimising the demands of generic drug manufacturers in the intellectual property debates and placing less attention to the agenda on generic drug regulation -- suggest that AIDS activists are giving the generic drug firms a free ride to further expand their stakes and reinforce the path of generic drug regulation in Brazil.

In summary, as the preferences of AIDS activists on the generic drugs are counterbalanced by the agenda on intellectual property, and as public pharmaceutical factories continue to adapt to the regulatory context, they both contribute to the path dependence process. With less resistance and weaker counter-reactions, AIDS activists and public producers also allow the trajectory of this regulatory policy to go further along the way.

## **Conclusion**

This first part of this chapter revisits the research problem and summarises the empirical findings. The second section discusses the theoretical and global health implications of these results. Finally, the third section reflects on the limits of the study and avenues for further investigations.

### **The research problem revisited and empirical findings**

In exploring the process of generic drug regulation in Brazil, it had been established that the Minister of Health and presidential hopeful, Jose Serra, promoted the reform as a response to a crisis in the pharmaceutical sector triggered by a scandal involving fake birth control pills (Dias 2003; Franca 2004; Dias and Romano-Lieber 2006). However, because previous studies only glossed over the antecedents to the reform and focused on the critical period of 1999 and 2002, little was known about the institutional antecedents and policy process that channeled Serra's entrepreneur activity. On the other hand, much has been said about the impact of Brazil's generic drug competition on the market and price structure (cf. Abreu 2004; Nishijima 2008; Quental et al. 2008; Rosenberg et al. 2008; Rosenberg 2009); however, there is hardly any evidence of its effects on actors' preferences and how this policy evolved in the 2000s. This is particularly intriguing, as a regulatory shift in the pharmaceutical sector might require the acquiescence of a number of participants in the policy process. Thus, this thesis aimed to assess Brazil's generic drug regulatory policy process, from its origins to the most recent developments. Apparently, no study has approached the generic drug regulation in Brazil from this perspective.

As opposed to studies of pharmaceutical regulation, which have tended to invoke firms and patient advocacy groups as drivers of regulatory decisions, or even the diffusion of regulatory guidelines (or best practices) as determinants of national regulatory developments, this thesis has proposed a theoretical construct that traces the historical development of the regulatory policy. Based on historical institutional analysis, it suggested that actors' preferences are constructed within the policy

process and that only by assessing the different stages of the generic drug regulatory process (reform and development) would it be possible to understand the choices for this policy option and its legacy. The research findings suggest the following points.

### **Findings on the reform determinants and actors' preferences**

It is well known that generic drugs have been an issue of intense political credit-claiming in Brazil, with the former Minister of Health, Jose Serra, openly publicising his protagonism towards the Generic Drug Act approved in 1999 and exploiting the political dividends associated with it. Additionally, previous studies of generic drug regulation have established that Jose Serra promoted the reform as a response to a crisis in the pharmaceutical sector (Dias 2003; Franca 2004; Dias and Romano-Lieber 2006). This thesis also acknowledged the role of the Minister of Health; however, it has suggested a more nuanced analysis. The first analytical exercise of this thesis was to assess the institutional antecedents during this eventful period of reform, focusing on actors' preferences and demands. This helped in understanding how and under what circumstances the policy preference for generic drug regulation was chosen in 1999.

Although there are records of the diffusion of the World Health Organization and support by other developed countries for the generic drug regulation in Brazil, they were not sufficient to promote a major change in the pharmaceutical sector regulation. Chapter 4 suggested that institutional legacies and contingent events gradually established the institutional trajectory of the 1999 reform. While the early attempts to introduce generic drugs in the 1990s had created an agenda for regulating off-patent medicines in Brazil, the introduction of intellectual property ensured that the regulation of off-patent medicines became essential. Both of these events highlight how the pharmaceutical sector in Brazil was poorly regulated and the government intervention deficient. How and when the regulation of off-patent drugs would happen was less evident. The third event refers to the HIV/AIDS epidemic. The Brazilian government was committed to providing universal access to the recently developed triple therapy used in the treatment of these patients, and the AIDS activism movement was keen to ensure that the government remained

accountable to this responsibility. Thus, the combination of patent protection in a context of universal access to HIV/AIDS treatment and an increase in the number of patients had major implications for the budget of the Ministry of Health in the late 1990s.

The crisis in the pharmaceutical sector triggered by the scandal surrounding fake birth control pills and the price of medicines, preceding the 2002 presidential elections, opened a window of opportunity to produce an otherwise unlikely policy change. The Minister of Health, Jose Serra, together with the government leader in the Chamber of Deputies, Ronaldo Cesar Coelho, and the first president of the recently created National Health Surveillance Agency, Gonzalo Vecina Neto, recycled the previous bills on generic drugs and began an intense lobbying process to have the policy approved in Congress. Their version of the bill 2022/91 was a not a creation of Brazilian officials; indeed, resolutions on how to regulate these products (e.g. approval guidelines) were already in place. Vecina and his team consulted academics and advisors from international agencies and observed how this policy worked in other countries. In this sense, arguments of policy emulation are not strictly wrong, but these were not a sufficient condition to initiate a reform. This is particularly evidenced by the failure to implement the WHO recommendation in 1993. Similarly, there is hardly any evidence of interest group activity in pushing the reform or supporting government intervention in their trademarks and manufacturing process; this contradicts explanatory perspectives that suggest the regulatory process, as captured by firms with an economic stake in the regulatory activity (cf. Stigler 1971). In other words, generic drug reform in Brazil was “politically driven”. The crisis in the pharmaceutical sector occurring in a particular point of the electoral cycle was vital to facilitate the political entrepreneurship of Jose Serra. Had Serra been a Health Minister in the early 1990s it is very unlikely that this reform would have been possible. As Chapter 4 demonstrated, the sequence of three events (Congressional effort to pass bill on generic drugs, the enactment of the IP law, and the AIDS epidemic) paved the way for the generic drug reform in 1999.

After the unanimous approval of the legislation by Congress in 1999, another step to promote the reform was necessary. The second stage of the generic drug reform referred to the technical resolutions and this was under the responsibility of the National Health Surveillance Agency. The study of Dias has explored in detail each of these resolutions (Dias 2003). This was a period of intense governmental activism to formulate the regulatory instruments and simultaneously induce a supply and demand for this product. Jose Serra was also responsible for proposing the creation of the Brazilian Association of Generic Drug Manufacturers (Pro-Genericos), which would secure the demands of firms in this sector. From the demand side, the government had promoted intense mass public campaigns to increase awareness about generic drug substitution aimed at stimulating a market for this product. All these decisions were discussed in detail in Chapter 4 and evidence a strong commitment of the Brazilian government to the reform.

The intention to regulate the off-patent pharmaceutical sector in Brazil caused distress and a period of high uncertainty for pharmaceutical firms. While multinational firms were concerned about the mandatory requirement to revise the display of their trademarks, local firms were concerned with the regulation as a whole (both the trademark alterations and the requirement for bioequivalence tests). During this period, it was not possible to find any interference by AIDS activists in the regulatory process, although they were particularly relevant in bringing the issue of pharmaceuticals to the agenda. An experienced politician and public manager, Jose Serra, utilised the crisis in order to promote his agenda in the media and requested that Congress investigate the structure of costs in the pharmaceutical sector (other examples were discussed in Chapter 4). The media fanfare would advance the crisis and stretch the latitude to implement his ambitious agenda. Furthermore, two unforeseen events (the currency devaluation and illegitimate market competition of pharmaceutical products that were not yet registered as generic medicines) added further cause for concern to the pharmaceutical sector environment. As Chapter 2 suggested, in a context of institutional vagueness, it is less viable for interest groups to behave strategically. Because future developments are to some extent unclear, it is difficult to choose which direction to pursue. Only by looking at the repercussions of



this policy is it possible to understand if there was a crucial change in the actors' stances and the policy path.

### **Findings on the evolution of preferences and policy development**

This thesis evolved to explain another stage of the regulatory process, that of policy development in the 2000s. Sustainability of generic drug regulation could not be immediately assumed for three reasons, as follows. Firstly, in general, pharmaceutical regulation would not be an object of a political partisanship agenda; however, the case of generic drugs was widely broadcasted as Serra's political proprietorship, an identity of his mandate as a Minister of Health that he had been keen on claiming credit for. Thus, the preceding administration could try to eclipse policy visibility or even reverse his decisions to lower the political advantage of generic drugs. Secondly, local pharmaceutical firms had voiced that the high costs associated with the new regulatory reform would limit their possibility to adapt to the reform and, if this was so, it could be expected that a movement demanding a reversal of generic drug regulation could emerge. Lastly, Brazil had unsuccessfully tried to introduce generic drugs in the past. This increased ambiguity about the future of this policy. All these factors enhanced the uncertainty about the path of the reform. As Peter Hall argued, "to be pursued effectively, any policy must be politically, as well as economically, viable" (Hall 1986: 280-1). As Chapter 2 has discussed, political viability in this case refers to the actors' support of a policy, which serves to legitimise it and push the trajectory further along. Thus, the aim was to assess the preferences and demands of selected actors on the generic drug regulation during the 2000s.

It has been suggested in Chapter 5 that the generic drug market in Brazil has increased by more than 350% since the reform, with an expansion of local pharmaceutical firms' competitiveness and a notable impact on the market structure and price (cf. Abreu 2004; Quental et al. 2008). However, this chapter has also claimed that government advocacy and market demand are inadequate to explain the development of generic drug regulation. While the government has been less politically active in this subject, market demand is still fragile. There is still much

suspicion among consumers and misunderstanding about the pharmaceutical products available in Brazil. Surprisingly, despite the remarkable concern regarding government intervention into their business, given the costs associated with it, local pharmaceutical firms have not just adapted to the new institutional context but become market leaders in this sector and strong advocates to maintain the policy path. This represents the second empirical finding of this thesis.

As the government demonstrated credible commitments to the reform, local pharmaceutical manufacturers began to adapt to the new institutional context. The policy process affected the feasibility of advocating for the previous economic preference, that is, the maintenance of a similar drug product. Despite the costs associated with the requirement to provide the bioequivalence tests (note that there were very few centres capable of producing these tests), to reformulate their products, labelling and marketing strategies, local pharmaceutical manufacturers adjusted their businesses to fit the new regulatory environment. Chapter 5 evidenced a reformulation in the interest group organisation in this sector, with the extinction of Abifarma and the creation of Pro-Genericos and Febrafarma to accommodate the new interests in this sector. Equally important, there was a possibility to adapt as these firms were proficient in Brazil's complex distribution channel. Given that multinational generic drug manufacturers were less able to enter the Brazilian market (either because of failure attempts or suspicions regarding the policy institutionalisation) there was latitude for local entrepreneurs to expand their business interests.

Thus, in 2003, when there was a chance for pharmaceutical companies to express their reaction to the generic drug policy, they opted not to. This was during the government deliberation to approve Resolutions 133 and 134 that decreed that all similar drug products must adapt to the bioequivalence requirements by 2014. There was no record of interest group activity to obstruct these resolutions; in fact, as recalled by a government official, local firms had already adapted and did not express any concern with these norms (Interview with government official B 2009). In contrast, Chapter 5 has described several policy debates in which local

pharmaceutical manufacturers have supported the use of INN and the relevance of bioequivalence tests to assure high quality products, which foster the country's industrial development. This contrasts starkly with the antecedent period, where these actors voice their concerns with government intervention. Finally, this chapter has also demonstrated that Brazilian firms are still strongly attached to an identity of generic drug manufacturers, despite their increasing potential in research and development activity. This is evidenced by their position in several intellectual property debates that have been taking place in Brazil throughout the 2000s, to revise or expand the Patent Act. By doing so, they reinforce the path of generic drug policy.

Yet, on the policy development process, Chapter 6 has analysed the position of actors that question the current architecture of pharmaceutical regulation in Brazil and the unforeseen consequences associated with the public production of medicines. Its conclusion represents the third empirical finding of this thesis, which refers to the consequences of this policy in relation to the public production of medicines. There is a concern with the option for bioequivalence tests and its connection to the concept of quality of medicines. Several publications consulted for this thesis have briefly questioned this frame and mentioned the struggle of public producers to adapt to it (PNUD 2006: 5; Gomes et al. 2008: 258; Hasenclever et al. 2008: 221). Furthermore, it has also been mentioned that, although some medicines produced in public factories are not bioequivalent, experts in pharmacology suggests that these drugs are more effective than their innovator versions (cf. Cassier and Correa 2003: 97). Nevertheless, to date no study explored has detailed the preferences and concerns with this aspect of the generic drug regulation. Data culled for this thesis suggests that, despite these concerns, there has been a movement of public producers to overcome the institutional constraints that limit their capacity to provide bioequivalence tests (e.g. public procurement of raw materials) and adapt to the new regulatory environment. This was discussed in Chapter 6.

On the other hand, AIDS activists have slowly initiated an agenda to discuss the relevance of bioequivalence, and of how and when it would be necessary. Their concern is that this scientific concept misleadingly associates generic drugs to quality

product (giving the impression that all other pharmaceutical products that are not bioequivalent as second standard) but in fact, it lifts the stringency of the regulatory norm, limiting market competition. With a concentrated number of suppliers, competition could be deficient. Similar concerns had been voiced by advisors of international organisations and international activists (cf. Gonzalez and Rossi 2004; Health Action International 2006). Nevertheless, Chapter 6 has suggested different reasons for the little leverage of their preferences and demands in Brazil. One refers to the difficulty in contesting the slogan of quality attached to the bioequivalence tests and the consensus around it. The second refers to their highly active agenda on intellectual property regulation, which might offset the advocacy in generic drug regulation.

This study concludes by stating that generic drug regulation in Brazil is currently supported by local pharmaceutical firms, despite their initial opposition in 1999. These local entrepreneurs successfully adapted to the new regulatory environment, reaping the benefits of a risky business turnaround. They have maintained their policy preference in favour of generic drug regulation during the 2000s, in spite of the few governmental investments in mass media campaigns to promote these products among the population and the reported suspicions of consumers (health professionals and patients). Had these firms not adapted, pharmaceutical regulation in Brazil may not have changed much since 1999, and there would still be competition between patented and similar products. It is difficult to predict what drug access prices might have been without a quantitative evaluation. Nevertheless, studies have demonstrated that generic drug competition in Brazil has lowered the price of medicines that treat many chronic diseases. By concluding that business actors currently uphold the generic drug regulation is not to say that they captured the regulatory process. What this finding suggests is that actors are not permanent opposers/supporters of a regulatory policy. Although the findings of a single case study are difficult to generalise, regulators of countries with a local pharmaceutical industry can diminish possible opposing sentiment to a generic drug policy by resisting to their pressures and creating trade policies that foster competitive industries. For instance, by negotiating market opportunities through

regional/bilateral trade agreements and providing the industrialists with technical and financial adjustment support, regulators might be able to bargain the support of local pharmaceutical firms and enhance the quality and supply of important generic drugs.

The second relevant finding of this thesis refers to the content of the generic drug policy. Although this regulation was introduced in Brazil in 1999 out of necessity to improve the quality standards of pharmaceutical products, those most vigorous supporters of access to medicines in Brazil, the HIV/AIDS NGOs, are critical of it today, citing that its stringency might limit the number of suppliers. Brazil has produced non-bioequivalent antiretroviral medicines for more than two decades in public factories for the National AIDS Program. Significant improvement in the quality of life of AIDS patients has been reported despite the use of non-bioequivalent pharmaceutical products (associated with original medicines). The recent engagement of AIDS groups in the regulatory process further reinforces the empirical finding that actors' preferences are constructed within the regulatory process, but also underscores the limitations of changing the norms once they become path dependent. Because there is a consensus among suppliers on the regulatory norm enacted in 1999, it has been difficult for these groups to challenge the current state of affairs of generic drugs in Brazil. Countries willing to introduce bioequivalence tests into local regulatory norms should further deliberate with different groups of society (e.g. pharmacologists, firms, representatives of patients) which medicines should be required to provide them. These findings have several theoretical and global health implications.

### **Theoretical implications**

This section revisits the theoretical parameters proposed in this thesis. As discussed in Chapter 1, the study of pharmaceutical regulation usually revolves around the regulatory norm as the triumph of interest groups over governments, or on the diffusion of international guidelines to regulate the sector (cf. Abraham 2002; Carpenter 2004; Abraham 2007; Abraham 2008; Carpenter 2010). However, the social process discussed in this thesis did not fit these two constructions. By contrast,

it suggests that institutional evolution, unexpected events and government actors had an important role in shaping the generic drug reform in Brazil.

Certainly, Brazil did not invent a generic drug regulation and, as previously discussed, this policy has its roots in the US FDA and subsequently diffused by the World Health Organization as a strategy to foster market competition, lower the price of medicines and consequently increase access to medicines. Although WHO and the US FDA have provided a stimulus for the reform, what this study has demonstrated is that domestic political institutions and policy legacies in Brazil primarily mediated the reform's enactment and development. International pharmaceutical regulatory guidelines establish the parameters that are acceptable in a given sector but, in order to put them into practice, it is necessary to activate them. Any attempt to do so, particularly in the complicated regulatory environment of pharmaceuticals, places government and groups in a conflicting scenario. Thus, national domestic institutions help to explain why the idea of introducing generic drugs in Brazil did not catch on earlier. In other words, the finding of this thesis suggests that it is necessary to investigate primarily how policy legacies (e.g. regulatory regimes) affect the preferences and capabilities of interest groups in order to understand the extent to which these international guidelines in the pharmaceutical sector matter for policy development. It can be problematic to assume that there is only one way of promoting pharmaceutical regulatory reforms, to compel countries to adopt it and assume that institutional infrastructure to support this best practice will arise if there is a demand for it. For instance, why should such countries as Colombia, Bolivia and Nicaragua incorporate a generic drug policy as proposed by the World Health Organization if there is already competition in place between a patent and off-patent products (not bioequivalent)? Although the claim that institution matters is nothing new to institutionalism scholars, this finding suggests good news to health policy scholars concerned with the diffusion of stringent regulatory pharmaceutical norms that could (arguably) limit access to essential medicines. These international resolutions are important, but not sufficient, conditions to initiate a policy reform.

Similarly, as with policy diffusion arguments, the theoretical construct of regulatory capture explains less the case of Brazil. By contrast, the findings of this thesis provide strong support for core propositions aligned with historical institutionalism and constructivism theories. The results of this study evidence that large-scale pharmaceutical regulatory reforms might not always be as a result of powerful corporations' lobbying activities. State actors in this case provided an important push to the reform. However, as suggested by Pierson (2004), the entrepreneurship of the decision makers much depends on the political and economic context in which they advocate for a reform and the timing to promote it. Promotion of generic drugs in Brazil was only possible given the confluence of contingent institutional legacies (e.g. enactment of IP regulation in 1996) and contingent events (e.g. AIDS crisis and scandal of fake medicines). The presence of the international guidelines to regulate off-patent medicines indeed contributed as a policy guide to respond to the crisis but it was not sufficient to move the reform forward. It is equally important to understand how the reform became steady. Preference formation helps in explaining how generic drug regulation developed in Brazil.

This thesis suggests that the preferences of corporations that are supposed to capture the regulatory process in the pharmaceutical sector can be shaped by those processes themselves. It has demonstrated a clear shift in the preferences and demands of Brazil's pharmaceutical industries that probably would have been left out of analyses that assume an actor's identity as rational and fixed. Facing a major crisis in the pharmaceutical sector, these firms were compelled to abandon their trademarks and adapt their manufacturing process to the new regulatory environment. Regulation can affect "which companies enter the market, what services they offer, what investment they make and what strategies they pursue" (Vogel 1996: 261). Thus, although firms' preferences sustain the generic drug regulatory policy, this does not mean that they control the regulatory arena. Similarly, this thesis has highlighted how the unintended consequences of this reform on the production of medicines in public factories have called attention of the NGOs, who are learning how to act in this regulatory environment. AIDS NGOs were illiterate in the area of pharmaceutical regulation during the 1990s, but became remarkably active in both health and

intellectual property issues in the subsequent decade. Much of this shift in their behaviour was promoted by the State, who empowered and financed their advocacy agenda during the crisis in 1999, but they slowly learned the implications of the regulatory norm in possibly restricting the availability of quality, affordable medicines.

If, on the one hand, these results contribute to an understanding of the policy change and stability and provide an alternative model of interaction in the regulatory process than suggested by rational choice scholars, on the other it also contributes to studies of regulatory lobbying, which usually concentrate on business-government interactions. This study has gone a step further by including other participants of the policy process – the NGOs. In addition, the supply of medicines in Brazil is not constrained to national and multinational firms, but also includes public production of medicines, i.e. the government acts as regulator and producer. This adds an element of complexity to access actors' preferences, but is also an opportunity to further investigate preference formation across different actors. It was possible to observe that it is not just material interests that are voiced by pharmaceutical firms, as they have publicly demonstrated their concern with access to medicines and national development issues.

These results are analogous to the study of Sell and Prakash (2004), who claim that firms and NGOs have their share of principal beliefs and instrumental objectives. The Brazilian government has provided different opportunities throughout the 2000s for groups to express their interests on controversial regulatory issues (e.g. Congressional hearings and *amicus curiae*). Most of these issues referred to a sophisticated understanding of pharmacology that is naturally well-known by manufacturers of pharmaceutical products. However, NGOs have proved a remarkable ability and expertise with which to bargain on this topic; for instance, the discussion on polymorphism and second medical use. How these groups contribute to the policy process is not as a result of their size or wealth, but on their ability to persuade policy makers and the receptiveness of government departments/branches to their demands. Theoretically, this means two related social phenomena. Firstly, it



relates to theories that understand the state as both an autonomous actor and a structure - the core element of the institutionalism school (cf. Immergut 1998). Regulators can act independently to interpret public interest and the ways to achieve it. This is not to say that they ignore societal interest, but that their preferences cannot be merely reduced to private groups' interests (Vogel 1996). Government actors' interpretation is not neutral, however. Their decisions are based on (or constrained by) institutional capabilities and ideological biases (Vogel 1996). In this sense, how actors frame their demands and the constitutive role of ideas play an important role in this relation with government, and this relates to the other theoretical observation<sup>63</sup>.

The second social phenomenon refers to the overlapping agendas in pharmaceutical regulation and actors' multiple goals. As seen in Chapters 5 and 6, regulators and legislators are now discussing in Brazil important amendments to the intellectual property law that requires the participation of different groups of society, including not just research-based firms but also generic drug manufactures and NGOs. Because this study took a different point of departure than rational choice scholars, who understand preferences as given and ranked, it was possible to observe and explore the content of firms and NGOs' demands. Both sides of this debate have their share of social interests and government needs to balance between fostering innovation while guaranteeing a certain level of access to affordable medicines. As seen in this thesis, pharmaceutical firms and NGOs contribute to the construction of the normative frame and use similar strategies to reach decision makers. Theoretically, Brazil's experience contributes to models of dynamic models of preference formation that sees actors' behaviour as a function of domestic political variables (political structures determine not just how much influence groups have but also what policies they demand in the first place) (Hathaway 1998; Crystal 2003; Hall 2005; Woll 2008).

The study of Shadlen (2011) raised important concerns on the shift in the direction of local pharmaceutical firms' preferences with respect to intellectual property. Based

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<sup>63</sup> In Elster terms, actor's preference is defined as broad rationality (Elster 1983).

on a number of empirical evidences, the author suggests that local pharmaceutical firms (that were mainly producers of generic drugs) have gained important innovative capabilities. This new ability to produce innovator products could also change their support to the institutional arrangement that makes patent granting in Brazil stricter than other countries (as it involves both the Patent Office and the National Health Surveillance Agency). However, there are reasons to believe that this is still far from occurring. First, Chapter 6 has demonstrated that NGOs have been remarkably active in upholding and reinforcing ANVISA's prior consent arrangement. Second, Chapter 5 suggests that, from several interviews and documents, there is, to some extent, disagreement between national producers on which direction to take (particularly members of ABIFINA and ALANAC that comprise similar and generic drug producers). Third, government departments and branches also have different opinions on these matters. While INPI has set the agenda for reformulating several IP resolutions, ANVISA and the Ministry of Health are strong supporters of the permanence of prior consent and question the necessity of patents for second medical use and polymorphs. Today, these topics have been the object of heated discussions in Congress and are apparently far from being resolved. In sum, the institutional mechanisms that assure regulatory policies to be stable and credible (policy feedbacks) are the same as those that make it difficult to propose new rules that might be necessary to incorporate new technological developments. If a theoretical lesson can be learnt from Brazil's experience, it is that reducing the preferences of actors to fixed, material versus normative, will provide an overly superficial understanding of the pharmaceutical regulatory process. Without diminishing the relevance of the norm diffusion and interest group activity, the findings of this thesis enrich both perspectives. It emphasises the importance of observing how the issue at stake is being framed which, according to Hall (2005), is something partly under the control of actors themselves and partly dictated by the structure of public discourse about it.

## Global health implications

The findings of this case study can also provide insights into the ongoing global health deliberations. For decades, the World Health Organization has included in its guidelines the necessity of implementing generic drugs as a strategy to foster competition in the pharmaceutical sector and increase access to essential medicines (World Health Organization 1988; World Health Organization 2001). The terminology of off-patent pharmaceutical products has been adjusted throughout the time to incorporate various countries' idiosyncrasies, for instance the adoption of multisource pharmaceutical products to include products such as similar drugs (cf. Homedes and Ugalde 2005a). Nevertheless, the discussion on bioequivalence has been constricted to scientific deliberations (Meredith 2003; World Health Organization 2005). As suggested in Chapter 6, NGOs and advisors of international organisations have only recently contested the content of regulatory norm, with the episode of exclusion of antiretroviral drugs produced by Indian firms that did not provide a certificate of equality. The argument is not that this test is unnecessary, but the number of drugs that should provide them might be lower than the prescription of WHO.

Similar to Brazilian NGOs, advisors of international agencies have also expressed concern over the effect of this rule on developing countries. A World Bank study (Osewe et al. 2008: 31-32) reported the case of a Zimbabwean state-owned pharmaceutical industry, Varichem. Despite a capacity to produce eight HIV antiretroviral medicines at competitive prices, Varichem cannot export its products or supply the Global Fund (and any other international donor agencies that fund AIDS treatment). Because its industrial unit does not comply with international manufacturing practices, its products would not pass the WHO prequalification programme (that requires GMP and bioequivalence certificates)<sup>64</sup>. Also, a study of the UK Department of International Development mentions the case of Sri Lanka

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<sup>64</sup> The WHO prequalification programme provides several manufacturing criteria (based mainly on the WHO guidelines for pharmaceutical regulation) that firms must fulfil to be able to supply international donor agencies. The prequalification programme intends to coordinate and facilitate the assessment of the quality of products supplied by the donor agencies.

and how its local agency does not have the necessary expertise to carry out bioequivalent tests (inability to conduct controlled trials in humans, for example) and lacks statistical and pharmacology-trained staff. They suggest that, even when bioequivalence data is available to local pharmaceutical producers, the innovator product might not be commercialised in the local market in order to establish a comparative study. Thus, this can represent a market barrier for many local pharmaceutical firms.

Other advisors of the World Bank have urged that it would be inappropriate to assume that similar drugs have lower therapeutic efficacy than their original versions (Homedes et al. 2005). In countries such as Argentina, Chile, Colombia, Peru, Bolivia and Uruguay, similar drugs represent the highest percentage of sales volumes. Frequently, many policy makers, users and prescribing physicians consider the similar and generic products to be synonymous (*ibid*). Also, countries that have aggressively implemented Generic Drug Policies, like Argentina and Chile, are promoting the use of similar drugs when the original drugs are off-patent (*ibid*).

Over the past decade, the Pan American Health Organization (PAHO) and its member countries have worked closely to establish harmonised procedures to improve the quality, safety and efficacy of pharmaceutical products marketed in the region. Its Working Group on Bioequivalence has also raised concerns about the WHO guidelines on this matter, the extent to which might limit access to medicines and the necessity to test off-patent medicines that have been on the market already (Pan American Health Organization 2008). Participants of these meeting have agreed that there is a political and commercial component in this concept that should be further explored in the following conferences, but also at the Ministry of Health level (*ibid*) (see also Health Action International (2006: 36)). The findings this thesis explore these concerns, suggesting that that generic drug regulation can affect the structure and governance of the pharmaceutical sector, which in turn affects an actor's preferences and demands. This can have far-reaching implications for the price and supply of medicines. This is particularly important given that an estimated two billion people lack access to essential medicines globally. Because, in

developing countries, 50 to 90% of medicines are paid by patients themselves, affordable pricing is a core determinant of access to medicines in these countries (World Health Organization 2004). Additionally, pharmaceutical policy has sweeping effects on public health; for instance, it can limit or foster the supply of affordable drugs, or poorly-regulated products can cause abortions, malformation or even death. Thus, understanding the factors influencing the formulation and development of generic drug regulation is important normatively. This study has demonstrated that Brazil, through its regulatory reform process, has enhanced access to high quality, affordable medicines while preserving generic competition.

### **Limits of the study and direction for further research**

The previous sections highlighted important theoretical and global health contributions of this thesis. This section now turns to the limitation of the thesis and proposes the direction for further studies.

This thesis has proposed an ambitious research design, seeking a comprehensive understanding of the regulatory policy process and its participants' preferences. Incorporating government, patient group advocacy, business and consumers into the analysis required multiple sources of in-depth information. While culling information about government, business and patient advocacy was a relatively feasible activity, data on consumers' perceptions on generic drugs in Brazil was limited. Only an in-depth assessment of nationwide public opinion polls could inform the perception of health professionals and consumers on this policy. Studies on policy feedback has suggested that public policies might have enduring effects for particular groups of society (e.g. providing resources or encouraging the organisation of certain groups), which reinforces the policy path (Campbell 2003; Mettler and Soss 2004). Thus, further studies should explore public opinion over this matter as they would allow a better understanding of the demand in relation to policy stability.

The option for a single case study research design naturally implies limitations as much as the generalisation of the research findings. However, this qualitative, crucial

case of generic drug regulation in Brazil provided detailed information on the process of policy reform and development. It complemented well established approaches to study pharmaceutical regulation and as suggested additional elements (e.g. institutional legacy and preference formation) to be taken into account when analysing pharmaceutical regulation. Comparative qualitative case studies on other countries that have implemented generic drug policy are necessary to give an understanding of the extent to which conditions such as intellectual property law, the WHO guidelines or crisis in pharmaceutical regulation give rise to new domestic regulatory norm, and also the extent to which actors' policy-reinforcement is concerned in policy development. Thus, it is necessary to investigate to what extent countries have converged in the direction of a common framework to regulate generic drug products and why there are national variations in these regulatory norms. For instance, it is crucial to understand how the politics of generic drugs evolve in contexts where co-payment and reimbursement systems are in place (as it is in the majority of European states). In these cases, government plays an important role in the demand of pharmaceutical products, different from developing countries. As the introduction of this thesis has mentioned, in developing countries access to medicines are mainly out-of-pocket or through fragmented pharmaceutical assistance programmes. How these institutional arrangements in the health sector affect the constituencies and political sensitiveness and mobilisation around this issue should also be considered. This thesis could possibly be the basis for other comparative institutional analyses related to developing countries' approaches to off-patent medicine regulations, a field yet under-researched.

The interdisciplinary nature of studies on pharmaceutical regulation is simultaneously a strength and weakness. These findings can inform decision makers on the institutional environment in which their decisions are taken, the groups and its demands/position on generic drug regulation and others. However, some specific elements of this public policy require further investigations. For example, it was not the object of the analysis to understand the extent to which the introduction of generic drugs has influenced access to medicines. This thesis infers, from data provided by market analysis consultancy and business association, that there was an

increase in the volume of sales of particular drugs and a decrease in price. However, access to medicines involves elements that go beyond the price of drugs and results from the interplay of economic and social factors, such as access to health care and family income (World Health Organization 2004). Only by conducting monitoring and evaluation studies will it be possible to understand the impact of this policy on access to medicines in Brazil. Similarly, assessing the post-marketing effect (pharmacovigilance) of generic drugs can also provide valuable information for health professionals and the population on the quality of these products.

Looking ahead, regulatory policy is a dynamic process, hence an object of constant monitoring and analyses for social scientists. Brazil's successful local generic companies have been the target of multinational generic and research-based pharmaceutical firms. As mentioned in Chapter 5, several acquisitions took place in the mid-2000s. Brazilian local firms have also gained innovative capabilities. The product of these hybrid corporations (producers of generic and original pharmaceutical products) is likely to bring fresh challenges to regulators. Currently, Brazilian officials are confronted with the question of how to regulate a new category of pharmaceutical products – the bioequivalent similar drugs, i.e. products that are equal to an innovator medicine but different from generic drugs and commercialised with a brand name. In the US, these are called branded generic drugs, but Brazil does not yet have a resolution on how to incorporate these products. This is crucial as, according to current norms, by 2014 all similar products must be adjusted to the Generic Drug Act, meaning they would need to either exclude their brand names or request a new patent (if eligible). A third alternative would be to promote new adjustments to the current regulatory path and, as this thesis has demonstrated, it can be a challenging task. As some issues raised in this concluding chapter suggest, understanding the implications of the generic drug regulatory process on an actor's preference and vice-versa should continue as an active area of intellectual inquiry.

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## **Annex 1. Interview protocol**

Interviews were non-standardized to allow flexibility in response. According to Dexter (2006 [1970]), in elite interviewing the investigator is willing to let the interviewee teach him/her about the problem, the question or the situation instead of relying upon the investigator's notion of relevance. There is no universal rule for conducting elite interviews; however I followed some guidelines suggested by the literature (cf. Richards 1996; Dexter 2006 [1970]), as follow.

Mostly I tried to schedule appointments at the respondent office or a place with limited interruption; avoiding having other persons that are not relevant in the interview setting to reduce distraction. The majority of interviews were conducted at the respondent's office but in some cases, particularly with business representatives, the conversation was arranged in a restaurant or coffee shop at lunch time. For others I had to conduct phone interviews because of distance or scheduling concerns. The process of scheduling interviews with high-level decision makers proved to be a fitness exercise. While businessmen and patient advocates showed a reliable agenda; politicians and government officials had a rather less reliable schedule. For some interviewees appointments had to be made weeks and sometimes months in advance but for others (e.g. the former health minister and governor of Sao Paulo state) I was supposed to be ready to get to his office at any time in a particular week. Additionally, in some cases the appointment was cancelled minutes before the interview. Besides these managerial decisions, once the interview started the majority of respondents were very receptive to answer all my questions.

At the beginning of each interview I presented myself, the institutions I was affiliated with, gave a brief explanation of my project and why the respondent was important to my research. I also explained ethical concerns and asked for verbal permission to record the conversation. Well-informed interviewees are usually unwilling to accept the investigator's assumptions and are willing to explain what real problems are as they view the matter (cf. Dexter 2006 [1970]). Interviews were semi-structured in

format to allow the respondent to speak freely about the topic. Sometimes this proved to be time consuming as some interviewees - particularly those who had long experience in pharmaceutical sector - began the conversation with a lecture of Brazil's pharmaceutical sector dating back as far as the 1930's. This required some intervention to focus the discussion on their perspectives over a particular element of pharmaceutical regulation. Most interviews lasted around 40-60 minutes but some interviewees were happy to speak longer. For example, an interview with a former representative of multinational pharmaceutical industries lasted more than 2 hours, when he gave me detailed information and documents about the process of generic drug reform. Similarly, an interview with a retired government official and high level decision maker on Brazil's trade policy took more than 90 minutes, when he provided relevant information about Brazil's industrial policy.

For each group of respondents I had a particular interview guideline. This research instrument was constructed and adapted as new data was collected<sup>65</sup>. Each interview was recorded and transcribed as soon as possible to guide the following investigations. I focused on the interviewee's frame and perspective of the problem we were discussing. For this reason it was particularly important to invest in documentary research / trial interviews and get a good deal of background information about the problem, thus avoiding having to focus on factual information during the interview. For example, there are some controversies about the process of generic drug reform. While multinational firms were constantly referred to in the media as trying to obstruct the reform, representatives of multinational firms assured that their interest was to invest in an awareness campaign parallel to the one been done by the government. Note that this debate had two versions; it was not the purpose of this study to investigate or solve this problem. However, my intention was to focus on how each side interpreted that process, their claims and observable strategies to convince the others.

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<sup>65</sup> A methodological note is relevant here as one could question the legitimacy of altering the data collection methods in the course of study investigation. As previously discussed, the aim of this study is not to produce summary quantitative data about a group of observations, but rather reflect and get as much information as possible about the case and social phenomena under investigation. "If a new data collection opportunity arises or if a new line of thinking emerges during the research, it makes sense to take advantage by altering data collection [...]" (Eisenhardt 1989: 539).

Normally I framed my inquiry with comments or questions that were quite open so the interviewee could interpret them in his/her own terms according to his/her experience. For example, 'In what ways are you most affected in your business practice by the federal department XXX?' or 'What people do you hear the most about the issue XXX?' The question order was also carefully considered. I began asking non-controversial questions to gain rapport and, move to more 'threatening' issues later on. Notes were also taken during and after the interview. I have paid particular attention to: a) interesting points the respondent suggested; b) particular ideas or problems of academic interest not related to my project (as this could be useful as the research moved forward); c) individuals or type of persons suggested that would be useful to contact. Finally, at the end of the interview I gave the interviewees an opportunity to talk about issues that I had not mentioned and that could be relevant. I also asked for references for further interviews and suggestions as to whom should I see first and later.

Finally, to increase validity and reliability I interviewed some respondents more than once (in person, by telephone or through written correspondence) to clarify uncertainties and ambiguities that became apparent after transcription and as new information appeared. I also used some additional strategies such as: cross-checking the information among different individuals and groups; asking the respondent to critique his own case (e.g. 'Why the government is not buying this idea?' or 'What would happen if the government decides to reformulate the generic drug act now?'); I also tried to get as much information as I could about the issue discussed before the interview and cross-referenced with documentary and quantitative evidence.



## Annex 2. List of Interviewees

Interviewee	Position
Alberto Goldman	Vice governor of Sao Paulo State and former Federal Deputy (1979-1982; 1983-1986; 1991-1994; 1995-1998; 1999-2002; 2003-2006)
Ana Paula Juca	Manager, Department of International Sanitary Regulation, National Health Surveillance Agency (ANVISA)
Carla Reis	Economist, Department of Pharmaceutical Products, Brazilian Development Bank
Carlos Codenzey	Director, Department of Economics, Ministry of External Affairs
Carlos Lessa	Former President of the Brazilian Development Bank (2003-2004)
Carlos Passarelli	Coordinator, Coordination of Technical Cooperation, Department of STD/AIDS, Ministry of Health
Célia Chaves	President, Brazilian Federation of Pharmacists
Dante Alario	President and Founder, Biolab Pharmaceutical Industry
Eduardo Costa	Former director, Farmanguinhos Public Pharmaceutical Industry (2006-2009)
Eduardo Jorge	Former Federal Deputy (1987-1991, 1991-1995, 1995-1999, 1999-2003)
Eduardo Martins	Former director, Farmanguinhos Public Pharmaceutical Industry (1989-1993)
Elisaldo Carlini	Former president, National Health Surveillance Agency (ANVISA) (1995-1997)
Eloan Pinheiro	Former director, Farmanguinhos Public Pharmaceutical Industry (1993-2003)
Fadlo Fraige	President, Brazilian Federation of Diabetes
Gabriel Tannus	Executive president, Brazilian Research-based Pharmaceutical Manufacturers Association (Interfarma)
Gaurino Gentil Jr	Specialist, Business Development, Merck S.A. Brazil
Gonzalo Vecina Neto	Former president, National Health Surveillance Agency (ANVISA) (1998-1999)
Gustavo Americano	Manager, Business Development, Merck S.A. Brazil
Henrique Moraes	Permanent Brazilian Mission in the European Union. Ministry of External Affairs
Jacob Frankel	Researcher, Federal University of Rio de Janeiro
Jaime Rabi	President and Founder, Microbiologica Pharmaceutical Industry
Jamil Haddad	Former Minister of Health (1992-1993)
João Sanches	Director of External Affairs, Merck Sharp & Dohme
Jorge Raimundo	President of the Advisory Board, Brazilian Research-based Pharmaceutical Manufacturers Association (Interfarma)
Jose Eduardo Bandeira de Mello	Former president, Brazilian Pharmaceutical Industry Association (Abifarma) (1993-2000)
Jose Miguel	Director, Department of Pharmaceutical Assistance, Ministry of Health
Jose Serra	Governor of Sao Paulo State and Former Minister of Health (1998-2002)
Liane Lage	Head of Chemistry Patent Division II, Brazilian Patent Office, Ministry of Development, Industry and Foreign Trade
Lucas Furtado	Former parliamentary assistant, Brazilian Congress
Luciana Capanema	Department of Pharmaceutical Products, Brazilian Development Bank
Luciano Lobo	Technical Coordinator, Brazilian Association of Generic Drug Manufacturers (Pro-Genericos)
Luis Eugenio Portela	Director, Department of Health Research, Ministry of Health
Luis Felipe Lampreia	Former Minister of External Affairs (1995-2001)
Luis Roberto Serrano	Journalist and former media assistant, Brazilian Pharmaceutical Industry Association (Abifarma)
Marcio Lobato	Diplomat, Department of Social Affairs, Ministry of External Affairs
Maria Del Pilar	Director of Institutional Affairs, Eurofarma Pharmaceutical Laboratory
Mariângela Simão	Director, Department of STD/AIDS, Ministry of Health

Marília Gomes	President, Brazilian Diabetes Society
Marta Fonseca	Head, Division of International Affairs, National Health Surveillance Agency (ANVISA)
Michel Lotrowska	Drugs for Neglected Diseases initiative (DNDi) and former Doctors Without Borders (MSF)
Nelson Brasil	1 <sup>st</sup> Vice-President, Brazilian Association of the Fine Chemistry, Biotechnology and its Specialties Industries (Abifina)
Norberto Rech	Associate Director, National Health Surveillance Agency (ANVISA)
Odilon Costa	Director of Institutional Affairs, Cristalia Pharmaceutical Industry
Odnir Finotti	Executive president, Brazilian Association of Generic Drug Manufacturers (Pro-Genericos)
Omlton Visconde Jr	Founder and former president, Biosintetica Pharmaceutical Industry  President of State of São Paulo Pharmaceutical Product Industry Syndicate (Sindusfarma)
Reinaldo Guimarães	Secretary, Secretariat of Science, Technology and Strategic Supply, Ministry of Health
Renata Reis	Coordinator of Working Group on Intellectual Property, Brazilian AIDS Interdisciplinary Association (ABIA)
Ricardo Oliva	Director, Foundation for the Popular Remedy (FURP) and President, Public Laboratories Association (Alfob)
Rosa Sampaio	Director, Coordination of Diabetes, Ministry of Health
Sergio Metzger	President of Brazilian Youth Diabetes Association (ADJ)
Silvio Albuquerque	Director, Department of Social Affairs, Ministry of External Affairs
Telma Sales	Director of External Affairs, EMS Pharmaceutical Industry
Vera Valente	Former manager, Department of Generic Medicine, National Health Surveillance Agency (ANVISA) (2000-2003)  Former president, Brazilian Association of Generic Drug Manufacturers (Pro-Genericos) (2003-2007)
Veriano Terto	Vice president, Brazilian AIDS Interdisciplinary Association (ABIA)
Zich Moyses	Director, Department of Health Economics, Ministry of Health

## **Annex 3. Consent form model**



**INFORMED CONSENT STATEMENT**  
**School of Social and Political Studies, University of Edinburgh, United Kingdom**  
**Elize Massard da Fonseca Doctoral Thesis:**  
**Political Sustainability of generic drug policy in Brazil**

### **INTRODUCTION**

You have been invited to participate in a research study affiliated with the School of Social and Political Studies, University of Edinburgh, United Kingdom. This study aims to explain the development of generic drug policy in Brazil.

### **DESCRIPTION OF PROCEDURES**

For this study, you will be asked to participate in one or more interviews with the principal investigator of this study, Elize Massard da Fonseca. Interviews will be carried out during the first semester of 2009 calendar year, and each interview will last approximately 40 to 90 minutes. Elize Massard da Fonseca may contact you for a subsequent interview to clarify uncertainties and ambiguities that could become apparent after transcription or as new information appear.

Topics you will be asked to comment on may include but are not limited to: you and/or your organization's role in the generic drug policy institutionalization and decision making process; changes on political/economic pharmaceutical sector environment after generic drug policy reform; and implication of generic policy for both local and multinational industry.

Interviews might be recorded to better analyze the research findings. You have the right to decline that the interview be recorded and/or request that your name not be attached to any of the study's findings.

You will be provided with a copy of the study's findings upon request.

### **RISKS**

Your participation in this study involves no physical risk.

### **BENEFITS**

If you decide to participate in this study there will be no direct benefit to you specifically. You may learn about development of Brazil's Generic Drug policy. You or your organization's role in development of this public policy may also be brought to light.

**EXTENT OF ANONYMITY AND CONFIDENTIALITY**

To ensure confidentiality, data will be stored securely and will be made available only to persons conducting the study.

**COMPENSATION**

Participants will not receive compensation for this interview.

**CONTACT INFORMATION**

If you have questions at any time about the study or the procedures you may contact the researcher, Elize Massard da Fonseca, at 21-26821103 or Dr Daniel Clegg, at the University of Edinburgh, +44-131-6503998. If you have any questions about the rights of research subjects or research-related injury, please contact Antonia Kearton at the office of the Research Ethic Committee, School of Social and Political Studies at +44-131-6513059.

**PARTICIPATION**

Your participation in this study is voluntary; you may decline to participate without penalty. If you decide to participate, you may withdraw from the study at anytime without penalty.

**CONSENT**

I have read the above information. I have received a copy of this form. I agree to participate in this study.

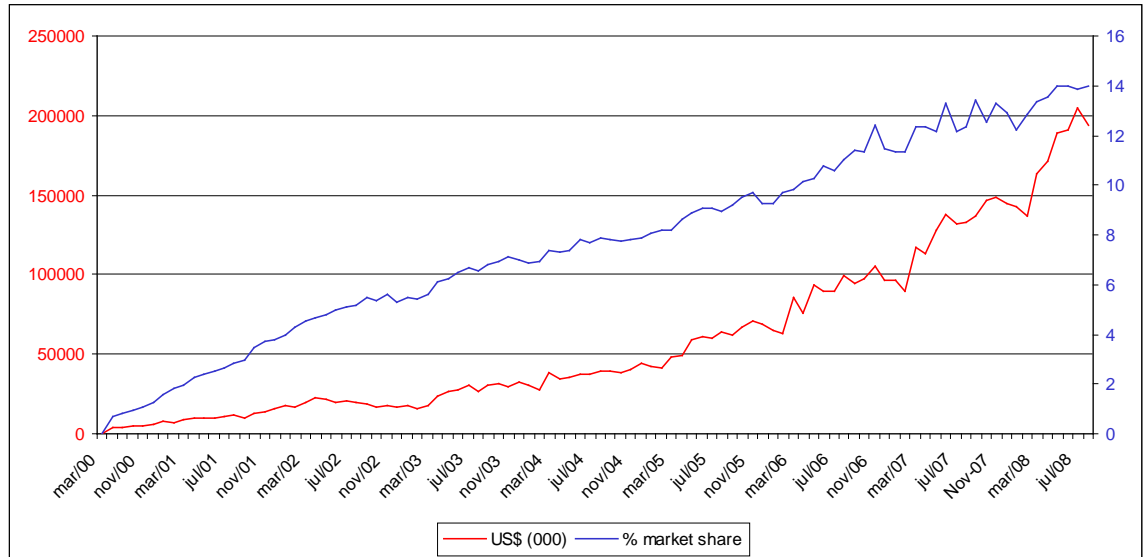
- I agree to have my comments recorded and quoted in publications.
- I agree to have my comments recorded but prefer that they not be quoted in publications.
- I do not agree to have my comments recorded or quoted in publications.

Participant's signature \_\_\_\_\_ Date \_\_\_\_\_

Investigator's signature \_\_\_\_\_ Date \_\_\_\_\_

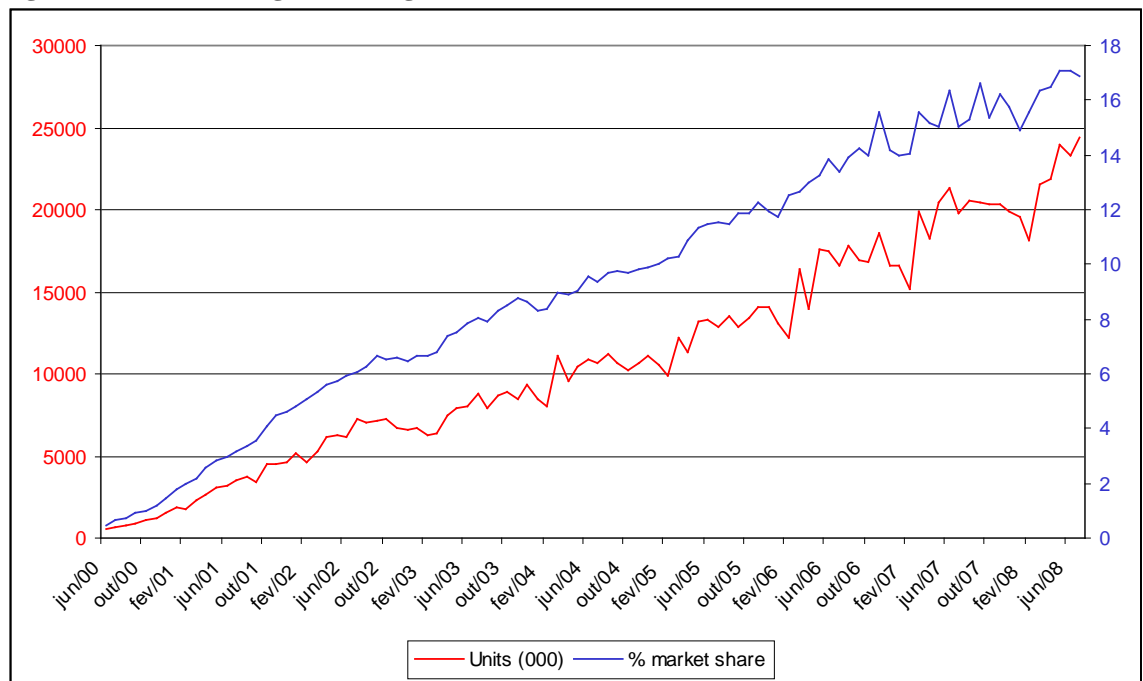
## Annex 4. Evolution of generic drug sector in Brazil

**Figure 9. Evolution of generic drug market in sales (US\$ 000). Brazil, 2000-2008**



Source: (Pro-Genericos 2009 - with IMS Health data)

**Figure 10. Evolution of generic drug market in sales (vol). Brazil, 2000 to 2008**



Source: (Pro-Genericos 2009 - with IMS Health data)

**Table 11. Index of generic drugs and total pharma. market (vol). Brazil, 2003-9**

	2003	2004	2005	2006	2007	2008	2009
Market total	1.261.555	1.257.373	1.319.652	1.374.574	1.463.288	1.556.291	1.658.695
Evolution index	100,00	99,7	104,6	109,0	116,0	123,4	131,5
Generic drugs	81.294	105.078	129.878	165.906	208.303	244.805	292.418
Evolution index	100,0	129,3	159,8	204,1	256,2	301,1	359,7

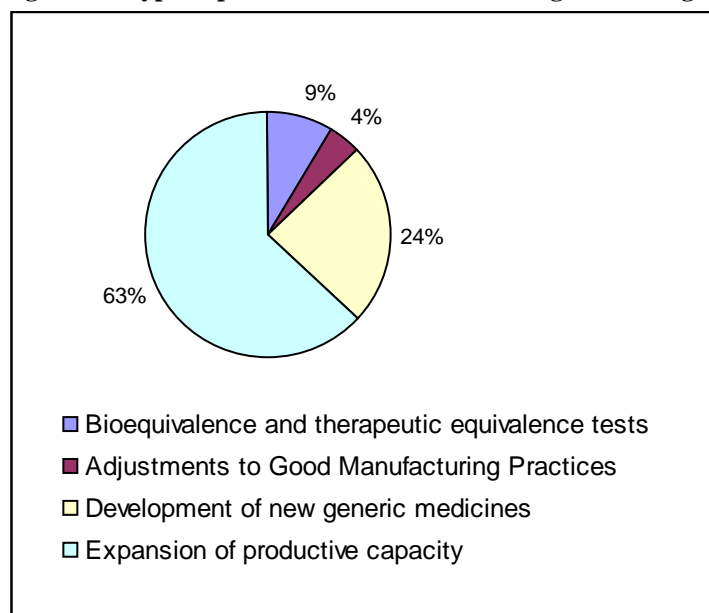
Source: (Pro-Genericos 2009 - with IMS Health data)

**Table 12. Index of generic drugs and total pharma. market (R\$). Brazil, 2003-9**

	2003	2004	2005	2006	2007	2008	2009
Market total	13.567.757	15.573.702	17.580.389	19.681.994	22.217.858	24.424.810	27.273.171
Evolution index	100,0	114,8	129,6	145,1	163,8	180,0	201,0
Generic drugs	728.075	1.067.504	1.393.024	1.850.410	2.528.603	3.136.644	3.891.830
Evolution index	100,0	146,6	191,3	254,2	347,3	430,8	534,5

Source: (Pro-Genericos 2009 - with IMS Health data)

**Figure 11. Type of private sector investments to generic drug manufacturing. Brazil, 1999-2004**



Source: (Pro-Genericos 2009 - with IMS Health data)

Note 1: Total investments between 1999 and 2004 US\$ 170 millions

Note 2: Forecast of investments until 2010 US\$ 354 millions

## Annex 5. Public-private partnerships enable 24 drugs to be produced nationally

State Laboratories	Private companies	Products	Treatment
Farmanguinhos	Globe	- Tenofovir	antiretroviral
	Chemo (Argentina),	- Budesonide - Formoterol+Budesonide	Asthma
	Lupin (India)	- Kanamicine - Cycloserine - Ethionamide - Ethambutol+Isoniazid+Pyrazinamide+Rifampicin	Tuberculosis
	Stragen Pharma (Switzerland), Bio-lab and Libbs	- Cyproterone+Ethinylestradiol - Desogestrel - Ethinylestradiol - Gestodene+Ethinylestradiol - Levonorgestrel+Ethinylestradiol	Contraceptives
Hemobras	Cristália	- Recombinant Factor VII-a	Haemophilia
LFQEX	Roche+Nor-tec	- Mycophenolate (mophetil), - Mycophenolate (sodium)	Immunosuppression
LAQFA	Libbs	- Tacrolim	Immunosuppression
Funed	Nortec Química, Blanver	- Tenofovir	Antiretroviral
Funed	Nortec Química, Blanver	- Atorvastatin	Cholesterol reduction
Funed	Not indicated	- Salbutamol	Asthma
Lafepe+Nuplam	Cristália	- Clozapine - Olanzapine - Quetiapine (Fumarate)	Antipsychotics

Source: Ministerio da Saude (2009a)