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PHARMACEUTICAL PATENT EXAMINATION IN DEVELOPING COUNTRIES

Lessons from Brazil

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DECLARATION

I certify that the thesis I have presented for examination for the PhD degree at the London School of Economics and Political Science is solely my own work.

This thesis was copy edited for conventions of language, spelling and grammar by Oxbridge Proofreading Ltd.

I declare that my thesis consists of approximately 52,076 words.

Eduardo Mercadante Santino de Oliveira

March 2025

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This was the hardest part of the thesis, so I will force myself to keep it to a single page.

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All my life, I have studied under scholarships.

May knowledge be open, equitable and revolutionary.

▼

Você pode até dizer que eu tô por fora
Ou então que eu tô inventando
Mas é você que ama o passado e que não vê
Que o novo sempre vem
...
Minha dor é perceber que apesar de termos
Feito tudo o que fizemos
Nós ainda somos os mesmos e vivemos
Como os nossos pais
BELCHIOR

▼

Mas sei que uma dor assim pungente
Não há de ser inutilmente
A esperança
Dança na corda bamba de sombrinha
E em cada passo dessa linha
Pode se machucar

Azar
A esperança equilibrista
Sabe que o show de todo artista
Tem que continuar

JOÃO BOSCO & ALDIR BLANC

▼

A tua piscina tá cheia de ratos
Tuas ideias não correspondem aos fatos
O tempo não para

Eu vejo o futuro repetir o passado
Eu vejo um museu de grandes novidades
Mas o tempo não para

CAZUZA & ARNALDO BRANDÃO

ABSTRACT

Since the enactment of the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), almost every country in the world has introduced patent protection for pharmaceutical inventions. However, there is considerable variation in the implementation of policies that address developmental and public health challenges. There is a wide agreement that developing countries should implement preventive (*ex ante*) measures to strengthen patent examination and promote balance in the public and private incentives in the patent system instead of relying on corrective (*ex post*) measures to address the negative consequences of lax examination. This thesis draws lessons about flexibilities in patent policy from the Brazilian experience of implementing pharmaceutical patenting since conforming to TRIPS in the late 1990s.

In 2018, Brazil started basing the examination in Brazil on reports published by other offices for applications covering the same invention, in a wide movement that seeks to simplify examination to expedite prosecution and reduce the backlog of pending applications. Chapter 2 shows that this has significantly increased the grant rate, and examiners tend to make fewer objections before issuing a grant. Combining these results with a comparison of grant rates with 14 other offices, the analysis concludes this approach has reduced the standard for granting patents in Brazil and produced more negative side effects than its intended goals.

Brazil also abolished the dual examination system where the patent office and the health regulator both had to examine pharmaceutical applications from 2001 to 2021, with the changing arrangements. Analysing the many arrangements for this system over two decades, Chapter 3 shows how the entities converged to high patenting standards and raised the scrutiny of all patentability criteria, especially invention description, despite the intense conflict over each entity's jurisdiction. Therefore, the regulator’s non-binding opposition to strategic applications contributed significantly to examination in an almost symbiotic relationship.

Lastly, Chapter 4 investigates the Brazilian government’s history of Hepatitis C drug procurement to assess the repercussions of these policies outside the patent office. Based on an understanding that the recommended treatments were equally effective and therefore great substitutes, the government shifted procurement to centralised tenders and induced competition by having originators of different drugs compete, regardless of each drug’s patent exclusivity status. Given the high patenting standard and originator’s commercial strategies, generic manufacturers could join those tenders, significantly boosting the government’s bargaining power. However, and tying together the three chapters, pressuring examiners to decide faster based on other patent offices’ reports and removing the dual examination system has led newer drugs to obtain patents more often, threatening the potential future benefits for the government of using this strategy of induced competition.

This thesis shows that Brazil has successfully explored policy flexibilities to strengthen examination but should be wary of policies that simplify examination to expedite prosecution, given the importance of promoting the balanced stimuli in patenting that generate positive externalities for public health strategies.

CONTENTS

LIST OF ABBREVIATIONS

Anvisa	National Health Surveillance Agency
CADE	Administrative Council for Economic Defence
CCD	Common Citation Document
CNPq	National Council for Scientific and Technological Development
CONITEC	National Committee for Technology Incorporation
Covax	COVID-19 Vaccines Global Access
DAA	Direct-acting antiviral
DNDi	Drugs for Neglected Diseases Initiative
EPO	European Patent Office
Fiocruz	Oswaldo Cruz Foundation
Furp	Popular Medicine Foundation
GATT	General Agreement on Trade and Tariffs
GDP	Gross domestic product
HCV	Hepatitis C virus
INPI	National Institute of Industrial Property
IPC	International Patent Classification
IPR	Intellectual property right
IP5	Five biggest patent offices
LAC	Latin American and Caribbean
LPI	Industrial Property Law
MedsPaL	Medicines Patent and Licence
MFN	Most-favoured nation
MoH	Ministry of Health
NACE	Statistical Classification of Economic Activities
OA	Office action
OLS	Ordinary least squares
PCT	Patent Cooperation Treaty
PDP	Partnership for Productive Development
PGO	Pre-grant opposition
PhRMA	Pharmaceutical Research and Manufacturers of America
PMA	Pharmaceutical Manufacturers Association
PPH	Patent Prosecution Highway

PPP	Purchasing power parity
R&D	Research and development
SUS	Unified Health System
TRIPS	Trade-Related Aspects of Intellectual Property Rights
UN	United Nations
USTR	United States Trade Representative
WHO	World Health Organisation
WIPO	World Intellectual Property Organisation
WTO	World Trade Organisation
3D	veruprevir/ritonavir/ombitasvir+dasabuvir

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1 INTRODUCTION

In 2023, pharmaceutical inventions were patentable in countries that together represented 81.5% of the world's population,[1] a stark change from a 1988 survey which found that pharmaceutical products were excluded from patenting in at least 49 countries, covering 65.5% of the world's population at the time (WIPO 1988). They could do so because the standard for intellectual property rights (IPRs) treaties served to preserve each country's capacity to adapt their patent systems to their particular socioeconomic, technological and developmental situation, including banning certain industries from patent protection. Since the enactment of the Trade-Related Aspects of Intellectual Property Rights (TRIPS) Agreement in 1994, excluding whole industries is no longer an option, but there is still considerable leeway for policy design. Therefore, the main question today is not if but *how* to implement pharmaceutical patenting (Correa 2000; 2022; Deere 2009; Abbot et al. 2013; Shadlen 2017; Shadlen et al. 2020).

This thesis focuses on how pharmaceutical patent applications are examined in a large developing country where the phenomenon is new: Brazil. The aim is to understand the flexibilities countries can use to promote balanced stimuli to innovation while addressing developmental needs and challenges. This thesis builds on the recommendation in the pharmaceutical patenting literature that developing countries should focus on strengthening patent examination as a preventive (*ex ante*) measure to avoid the negative effects of protecting inventions that do not merit patent exclusivity. This is an alternative to counting on the errors made by lax examination being fixed by corrective (*ex post*) measures like patent challenges in courts (Correa 2000; Drahos 2008; 2010; Shadlen 2013; 2017; Sampat and Shadlen 2015; Frakes and Wasserman 2023).

This thesis draws lessons from three case studies of pharmaceutical patent examination in Brazil. First, it analyses the trade-off between speed and quality in examination, considering 53,597 pharmaceutical applications prosecuted by the Brazilian patent office. Second, it investigates the grounds for 2,589 negative decisions. Third, it assesses how the interaction between patent exclusivity and therapeutic substitutability has affected the centralised procurement of drugs to treat patients with the Hepatitis C virus (HCV). This thesis uses these Brazilian case studies to illustrate how the pursuit of examination efficiency cannot be blind to

[1] Considering all members of the World Trade Organisation, except for least developed countries (UNCTAD 2024; OWID 2024; WTO 2021a).

the effects on quality, how cooperation between the patent office and the health authority can produce a surprisingly symbiotic relationship that increases patenting standards, and how the government may increase its bargaining power by making manufacturers of equally effective drugs compete for the same contract, producing significant price reductions especially when there are high granting standards for patents.

The remainder of this Introduction is divided into four sections. The first section defines the theoretical approach to patents and explains why the literature suggests that developing countries should be particularly careful with examining pharmaceutical patents. Next, a summary of the history of IPRs in international treaties shows how pharmaceutical inventions became patentable almost everywhere. Then, another section explains why Brazil is a representative case for this analysis. The final section defines the research questions, explains the empirical strategy of the three case studies, and summarises the main findings.

1.1 The balanced stimuli of patents

Hess and Ostrom (2003) define knowledge as a classic public good because its consumption is non-rival (being consumed does not reduce its stock) and non-exclusive (one person cannot prevent another from consuming it if both have access). Patents are one way to make knowledge partially excludable: only patentees or authorised third parties may commercially exploit the invention in the terms described in the patent for a certain period, creating what Polanyi (1944) would call a fictitious commodity, which promotes the appropriability of knowledge.

Machlup and Penrose (1950) identified four rationales for patenting, the first two from law, and the other two from economics: inventors have natural or moral rights over their ideas; inventors have the right to a reward for their talent; industrial progress depends on rewards for inventors' investments; and industrial progress depends on public knowledge disclosure. Combining the economic arguments, the challenge of patents is balancing the trade-off between the static costs of limiting who can exploit the invention and dynamic gains of investments incentivised by private rewards and public knowledge disclosure (Nordhaus 1969).

Balancing the private and public incentives of patents is as difficult as it is necessary. If enforcement is too weak or too costly, patentees are unable to protect their interests, losing the incentive to share their knowledge or even to develop the inventions at all. However, there

are questions over who should be rewarded, given the cumulative character of knowledge, and whether patents exaggerate or underestimate the reward to the inventor (Chang 2001; Macdonald 2002; Granstrand 2005; Andersen 2006; Rockett 2010).

Patents are a classic case of barriers to entry which could reduce competitiveness and, consequently, social welfare. They could also promote overinvestment in technological paths that are most likely to be patentable, creating a system that biases investments to the instrument (patent) instead of focusing on the result (innovation). Patents may also lead competitors to make potentially inefficient investments in substitute innovations, especially when granted too early in the technological trajectory (Winter 1993; Cohen, Nelson and Walsh 2000; Chang 2001; Macdonald 2002; Granstrand 2005; Andersen 2006; Rockett 2010).

According to Arrow (1962, p. 618), '[i]nformation is not only the product of inventive activity, it is also an input – in some sense, the major input apart from the talent of the inventor'. Thus, how much knowledge is codified in the patent documents influences the effectiveness of patent protection (Teece 1986). Patents cannot protect uncodifiable or tacit knowledge. Also, while patents can only protect what is described in the documents, leaving important parts out makes it harder for competitors to copy the invention (Cohen and Levinthal 1989). Thus, inventors may withhold the knowledge that cannot or need not be described in patent documents (Cowan, David and Foray 2000). As a result, there is a dilemma between describing knowledge to protect it or keeping it secret to increase the cost of copying.

Naturally, this dilemma is influenced by the scope and length of patents. Kitch (1977) proposed granting broader patents to promote the development of more disruptive inventions, which have higher costs and failure rates. However, Horowitz and Lai (1996) suggested that the length that maximises innovation is longer than that if the goal is to maximise social welfare, which is caused by longer patents increasing the size but decreasing the frequency of innovation. Others argue that, in some sectors, the benefits of incremental innovations might outweigh the gains from granting broader protection to the pioneer (Merges and Nelson 1990; Mazzoleni and Nelson 1998). If patent terms can differ depending on the sector, Klemperer (1990, p. 127) proposed that:

> *Infinitely lived, narrow patents are typically desirable when substitution costs between varieties of the product are similar across consumers, but very short-lived, wide patents are desirable when valuations of the preferred variety relative to not buying the product at all are similar across costumers*.

Another common criticism of the patent system is that it is not equally useful across all industrial sectors and that other forms of IPRs might be more effective for other industries (Pavitt 1984; Mansfield 1986; Levin et al. 1987; Cohen, Nelson and Walsh 2000; Cohen et al. 2003; Hall et al. 2014). For example, if knowledge is highly codifiable and the costs of copying are lower, trade secrets might be better because the knowledge is not shared publicly.

Moving from IPRs in general to pharmaceuticals specifically, various characteristics of the pharmaceutical industry explain why it is a classic example of a sector that benefits from the patent system (Pavitt 1984; Bell and Pavitt 1993; Achilladelis and Antoniakis 2001; Hasenclever et al. 2010; Scherer 2010). First, imitation is generally easy (especially in synthetic pharmaceuticals), so innovators have a strong interest in obtaining patents to block this. Second, knowledge is reasonably easy to codify in patent documents, so patents can be an effective appropriation method. Third, technologies have a longer life cycle, so securing exclusivity for at least 20 years is more important. Fourth, demand is often price-inelastic because patients are highly motivated consumers; they need the treatments. Fifth, the costs related to research and development (R&D) are very high, so investors want to secure high rewards. Sixth, there is a high R&D failure rate, so the profits from one product must cover its production costs and the costs related to failed products. Seventh, the broader scope and longer protection periods significantly increase the artificial barriers to entry and market shares.

Given these challenges in balancing the stimuli created by patents, it has been proposed that countries should implement policies that address the possible examination errors and their consequences, especially for pharmaceutical inventions in developing countries (Correa 2000; Drahos 2008; 2010; Shadlen 2013; 2017; Sampat and Shadlen 2015; Frakes and Wasserman 2023). A lax patent examination can lead to granting what should be rejected or rejecting what should be granted, and the recommendation of preventive measures is especially worried about the former. The challenge of avoiding mistakes is influenced by the patent office's resources, which are more limited in developing countries. These countries also tend to have less regulatory capacity to correct mistakes, given the asymmetries in the economic and legal power. On top of that, pharmaceutical markets are especially sensitive to these mistakes due to socioeconomic and industrial challenges. Since many countries had to begin examining pharmaceuticals after signing TRIPS and this industry is highly interested in obtaining patents, patent offices may get overwhelmed with the new influx of applications they have little or no experience examining, increasing the chances of examination errors.

This thesis treats patents as a public policy in which patentees receive temporary exclusivity in commercial exploitation in exchange for public and sufficient knowledge disclosure, generating gains for society that compensate for limiting competition. Thus, patents should incentivise innovation by rewarding the inventors' investments and publicly disclosing inventive knowledge, generating dynamic incentives for further innovation. However, there should be a balance between these private and collective stimuli to prevent disincentives to private investments and to mitigate the anti-competitive effects that restrict social welfare, considering the variation in the effectiveness of patents as appropriation strategies across industrial sectors. This thesis follows the suggestion that developing countries cannot rely on corrective (*ex post*) measures, such as patent challenges in courts. Instead, they should strengthen the work of patent offices as preventive (*ex ante*) measures against such errors.

1.2 The push for and against pharmaceutical patenting

Historically, IPRs have been used not only as incentives and rewards for creativity but also as mechanisms of patronage, creating monopolies for particular individuals or organisations, or as protectionist measures to promote socioeconomic and industrial development (Chang 2001; 2002; May and Sell 2006; Clift 2010). However, this strategic use has been progressively restricted over the last 150 years, in a process marked by three factors summarised by May and Sell (2006, p. 107) as 'shifting ideas or conceptions of ownership, authorship and invention[,…] changes in the organization of innovation and the production and distribution of technology [… and] institutionalization of these changes in law'.

In the 19th century, industrialisation and expansion of foreign trade intensified disputes over IPRs. This state of uncertainty culminated with inventors from the United States refusing to attend the World Exposition in Vienna in 1873 over the fear of their inventions being copied in a country where they could not obtain protection, despite this being part of the United States' industrialisation strategies. As a result, the Paris Convention for the Protection of Industrial Property was adopted in 1883 as the first multilateral IPR treaty, forbidding the discrimination of applicants based on their nationalities and creating a system for filing applications covering the same invention in multiple jurisdictions while keeping the same date for the analysis of novelty and inventiveness. However, the Convention was a voluntary commitment, did not determine how protection should be implemented (e.g., for which inventions or for how long), and had no enforcement mechanism (Chang 2001; 2002; May and Sell 2006).

Pressure for stronger international IPR institutions grew in the 20th century as a response to technological development, economic integration, complementarities between IPRs and financial markets, and new asset structures based on higher industrial and technological innovation patterns. The biggest proponent of strengthening IPR institutions was the United States, influenced by intense lobbying from its knowledge-based industries, especially the Pharmaceutical Manufacturers of America (PMA).[2] It was proposed that the country use IPR protection to exploit its competitive advantage in these sectors and reverse the growing trade deficit. Internationally, these efforts were reflected in the branding of counterfeit products as piracy, which is an allegorical example of how IPRs were forced into the trade arena (Drahos 1995; Chang 2001; May and Sell 2006; Orsi and Coriat 2006; Clift 2010; Coriat and Weinstein 2012).

This movement was met with resistance, mainly from developing countries. Many argued that IPR issues should be kept within the realm of the World Intellectual Property Organisation (WIPO), created in 1967, which is historically oriented towards arbitration and does not have enforcement powers. These proposals were modelled on the IPR regimes of developed countries, which were seen as inappropriate for developing countries, and opponents of the proposals faced direct commercial retaliation from the United States Trade Representative (USTR) through the Special 301 reports. In simple terms, these three-tiered annual reports indicate countries where the USTR is aware of possible infringement of the IPRs of United States nationals, is concerned about infringement or is convinced infringement is happening. This leads to mandatory trade sanctions. Countries' positions in the Uruguay Round of the General Agreement on Trade and Tariffs (GATT) were used by the USTR to justify placing them in one of the tiers, which meant dozens were listed and 12 were even sanctioned during the negotiations (Drahos 1995; Chang 2001; May and Sell 2006; Orsi and Coriat 2006; Deere 2009; Clift 2010; Shadlen 2017).

This process culminated in a paradigm shift for international IPR institutions in 1994, at the end of the Uruguay Round. It produced an agreement establishing the World Trade Organisation (WTO) and several annexes, one of which was the TRIPS Agreement. Negotiated as a single undertaking, the WTO agreement was achieved through what Steinberg (2002) calls the 'power play' of the United States and the European Community, making signing the agreement a condition to access their markets under most-favoured-nation (MFN) status, thus

[2] In 1994, this group was rebranded as the Pharmaceutical Research and Manufacturers of America (PhRMA).

receiving any advantage given to other partners. While most developing countries were against the TRIPS Agreement, many would benefit from other subsidiary agreements negotiated in the Uruguay Round and so to obtain access to most markets and the gains offered in the annexes of the WTO Agreement, countries had to agree to everything (Drahos 1995; Chang 2001; May and Sell 2006; Orsi and Coriat 2006; Deere 2009; Clift 2010; Shadlen 2017).

Notwithstanding the hard work of the few developing countries like Brazil and India which had qualified representation in the Uruguay Round discussions in blocking some very restrictive dispositions, the TRIPS Agreement differed significantly from the Paris Convention in four ways. First, signing it was mandatory for countries that wished to join the WTO. Second, it imposed several minimum standards of IPR protection. Third, it determined specific transition periods depending on income level. Fourth, it is not governed by WIPO as other IPR conventions and treaties are, but by the WTO, which has strong enforcement power (WTO 1994; Drahos 1995; Chang 2001; Clift 2010). Therefore, 'TRIPS was primarily the means for this key neoliberal project of constructing a global regulatory architecture suitable for the marketization of knowledge' (Tyfield 2016, p. 344).

Perhaps the most significant change introduced by TRIPS for this thesis was the prohibition of sectoral discrimination, meaning no country could exclude a particular industry from patenting by determining that 'patents shall be available for any inventions, whether products or processes, in all fields of technology' (WTO 1994, Art. 27.1). In 1988, WIPO surveyed the restrictions on patenting in 97 members of the Paris Convention and found that the most common restriction was on pharmaceutical products, which was limited in half of the countries, including some developed nations (WIPO 1988). TRIPS determined that developed countries had to reform their patent systems immediately after the signature while low- and middle-income countries had until 2000 to finish most reforms and until 2005 to introduce patenting to previously banned sectors. The deadline for least developed countries has since been extended twice and currently ends in 2034 (WTO 2021a).

Notwithstanding the unprecedented level of mandatory requirements, also called 'TRIPS-minimum' dispositions, there have been moves to increase and relax the level of protection. The push for 'TRIPS-plus' dispositions is normally done in free-trade agreements, where developed countries demand stronger protection measures that expand the duration, scope and power of IPRs. However, many have urged countries to explore the flexibilities within TRIPS regarding which, when and how inventions are patentable to counterbalance the

effect of increased protection from TRIPS-minimum and TRIPS-plus dispositions, especially in developing countries (Correa 2000; 2014; 2022; Deere 2009; t' Hoen et al. 2018; Shadlen 2017; Shadlen et al. 2020; Tenni et al. 2022).

The TRIPS Agreement recognises the right to 'adopt measures necessary to protect public health' (WTO 1994, Art. 8). In 2001, the Declaration on the TRIPS Agreement and Public Health reaffirmed that:

> *The [TRIPS] Agreement can and should be interpreted and implemented in a manner supportive of WTO members' right to protect public health and, in particular, to promote access to medicines for all [by using], to the full, the provisions in the TRIPS Agreement, which provide flexibility for this purpose" (WTO 2001, Art. 4).*

Recently, this topic gained greater prominence with calls led by developing countries for IPR waivers during the COVID-19 pandemic (WTO 2021b; Fischer et al. 2024).

In summary, the post-TRIPS paradigm of international IPR protection is far from what it was in the Paris Convention. Until the end of the 20th century, most countries had some exclusions to the patenting of pharmaceutical products, but the world has since moved into an era when it is no longer necessary for lobbying groups such as the PMA to push for the protection of pharmaceutical inventions. Instead, the challenge is for countries to explore the flexibilities within the new international arrangement. This thesis draws lessons from the implementation of pharmaceutical patenting in Brazil about policy flexibilities so that patents can fulfil the goal outlined in Section 1.1 of producing balanced public and private incentives.

1.3 Trailblazing patent policy in Brazil

The history of Brazilian IPR legislation shows how much of a trailblazer the country has been. In 1809, Brazil became the fourth nation to enact specific legislation for patents (at the time, called 'privileges') as one of the policies implemented by the Portuguese court after relocating to Brazil to escape Napoleon's advance on the colonial metropolis. In 1822, the first patent was granted to Luis Souvain and Simão Clothe for a machine that peeled coffee beans (Arquivo Nacional 2021). Since the goal was to create an advantage for Brazil, patents were only granted to nationals, required local production, and could be revoked if the applicant tried to protect the invention elsewhere. However, the general opinion changed over the decades,

with the first patent to a foreigner being given to Thomas Edison in 1878 for the invention of the phonograph, before the Paris Convention established the national treatment (Barbosa 2013). As a result, Brazil was an active negotiator and one of only 10 countries that signed the Paris Convention in its creation, before even the United States (WIPO 2024a).

Pharmaceutical inventions were patentable since 1809, making Brazil one of the first countries to do so. In 1882, the country also introduced a system where the Central Board of Public Hygiene would have to give prior consent to the grant of pharmaceutical patents. Thus, Brazil was already exploring IPR policy design even before the Paris Convention. However, as developmental ideologies gained strength in the country, so did the opposition to the internationalisation of the patent system and, eventually, the system itself. Domestically, an important consequence was the exclusion of pharmaceutical products in 1945 and processes in 1969. Internationally, Brazil stopped adopting the updates to the Paris Convention after the 1925 Hague version and started leading a movement in the United Nations (UN) to challenge the role of patents for developing countries (Barbosa 2013).

Brazil was one of the foremost opponents of bringing IPR matters into the trade arena under the WTO, proposing to keep it under WIPO to preserve the capacity to use IPR policy to address socioeconomic and technological challenges that were more significant for developing countries. As one of the few developing countries with delegates that specialised in IPRs, Brazil had a prominent role in international forums, especially during the Uruguay Round (dos Santos Tarragô 2015). This international leadership, along with the protectionist policies, led Brazil to become a direct target of the United States. In 1985, sanctions were imposed because Brazil reserved a share of the computer market for national companies and introduced what was seen as weak protection rights for software. In 1987, the PMA successfully lobbied the United States government to impose sanctions because of the exclusion of pharmaceuticals. This sanction happened shortly after Brazil spoke against the United States' proposal in the Uruguay Round and was announced on the Brazilian Independence Day, September 7th. The sanctions only ended in 1990 after recently-elected president Fernando Collor de Mello went to Washington and promised to reintroduce patenting to pharmaceutical products and processes, and, once in office, created an interministerial group to amend the patent legislation, introducing a decade of neoliberal policies that went beyond IPRs (May and Sell 2006; Deere 2009; Clift 2010; Barbosa 2013; Fonseca and Bastos 2016; Shadlen 2017; Reis 2022).

In 1996, Brazil promulgated the Industrial Property Law (LPI) after five years of intense debate. The debate was marked by intense lobbying from foreign powers to increase IPR protection and fierce opposition from civil society and national industry associations. As a result, Brazil is one of the most common case studies of IPR policy design in the 21st century because of the TRIPS-plus and flexibilities it implemented (May and Sell 2006; Deere 2009; Barbosa 2013; Fonseca and Bastos 2016; Shadlen 2017; Reis 2022).

The LPI made Brazil fully TRIPS-compliant in 1997, when it started examining pharmaceutical applications. This is a TRIPS-plus disposition because Brazil could have waited until 2000 to reform the legislation and until 2005 to begin examining pharmaceuticals.[3] During this transition period, TRIPS required countries to accept applications for pharmaceutical products, which would be examined after the transition. This mechanism, known as mailbox, was not extended to process patents. Therefore, by anticipating the reform, Brazil had to accept process applications and examine all applications in 1997, when this could have been delayed until 2005.

A second TRIPS-plus mechanism was the automatic patent term extension clause. The LPI followed TRIPS in determining that patents were valid for 20 years from filing. It also stipulated that terms would last for at least 10 years from the grant. Thus, when the Brazilian patent office, known as the National Institute of Industrial Property (INPI), took more than 10 years to grant a patent, the term would automatically be extended by that much regardless of what caused the delay or how big it was. In 2021, the Brazilian Supreme Court decided this automatic extension mechanism was unconstitutional (STF 2021).

From the promulgation of the LPI, there was a one-year period of *vacation legis* during which applications from previously excluded technical fields – such as pharmaceuticals – that had been filed elsewhere could also be filed in Brazil through the pipeline system, another TRIPS-plus element. Pipeline patents were only screened for formal requirements and could be issued without substantive examination if they had also been granted elsewhere, if the invention had not been marketed anywhere, and if there was no significant effort to develop it in Brazil. The patents had a 20-year term from the filing of the foreign application that had been granted, without the extension due to prosecution delays. Effectively, this was a way to appease the pharmaceutical lobbying groups by patenting older drugs whose developers could

[3] This thesis focuses on pharmaceuticals, but some aspects of the TRIPS Agreement have implications for other industries previously excluded from patenting in Brazil such as agrochemicals.

not have applied for applications in Brazil when they were invented (Barbosa 2013; Shadlen 2017; Reis 2022).

Brazil also enjoyed some flexibilities that reduced the expansion of IPRs and strengthened the social rewards. As flexibilities explicitly named in TRIPS, the LPI determined some exclusions to pharmaceutical patenting including parts of living beings or diagnostic, therapeutic and surgical methods, non-commercial uses that do not configure patent infringement such as the Bolar Exception (or 'early-working' provision) which allows the non-commercial use of objects of inventions for research and trials, the conditions for compulsory licensing, and mechanisms for pre- and post-grant opposition (Shadlen 2017; Mercadante and Paranhos 2022; Reis 2022).

Lastly, the most significant flexibility that Brazil introduced regarded how patent applications are examined. Instead of having just the INPI's opinion, the LPI introduced a provision in 2001 requiring pharmaceutical product and process patents to receive consent from the health authority, the National Health Surveillance Agency (Anvisa), before being granted by the INPI. This requirement followed the 1882 precedent of requiring consent for pharmaceutical patenting. From 2001 to 2021, both entities examined applications, but there were constant conflicts and high uncertainty about jurisdictions and the consequences of negative decisions. While some argue this policy was introduced to help the INPI because it had to examine pharmaceutical applications for the first time since its creation in 1970 (Silva 2008; Abreu 2017), others claim that it was designed as or developed into a way to prevent granting secondary patents, especially since given the pipeline mechanism (Shadlen 2011; 2017; Guimarães and Corrêa 2012; Correa 2014; Sampat and Shadlen 2015; 2017).

Based on the two centuries of pharmaceutical patent legislation revised in this section, Table 1.1 summarises the most important changes for this thesis.

Table 1.1. Timeline of key changes in pharmaceutical patent legislation in Brazil

1803	First specific legislation for patenting, including pharmaceutical inventions.
1882	Pharmaceutical inventions can only be patented after a consent from the Central Board of Public Hygiene.
1883	Signature of the Paris Convention.
1945	Exclusion of pharmaceutical products from patenting.
1969	Exclusion of pharmaceutical processes from patenting.
1994	Signature of the TRIPS Agreement.
1997	End of the harmonisation process to the TRIPS Agreement, reintroducing patenting to pharmaceutical products and processes, and including TRIPS-plus dispositions (e.g. pipeline and patent term extension mechanisms) and TRIPS flexibilities (e.g. Bolar Exception and compulsory licenses).
2001	Pharmaceutical inventions can only be patented after a consent from Anvisa.

Notwithstanding this history of international leadership and creative IPR policy design, one could propose Brazil as a case study purely on socioeconomic statistics, as summarised in Table 1.2. Summary of socioeconomic and innovation statistics about Brazil. The country has the 7th biggest population and gross domestic product (GDP) in purchasing power parity (PPP) but only the 86th highest GDP per capita. It is 89th on the Human Development Index, with a higher inequality than the averages for other countries with high human development and for the Latin American and Caribbean (LAC) region. Brazil is also the 50th economy in the Global Innovation Index, leading the LAC region. The INPI is one of the biggest offices in annual applications (10th) and grants (8th), especially for pharmaceuticals (9th and 8th). However, Brazilians are much less prominent as applicants considering all technical fields (23rd and 25th) despite performing slightly better with pharmaceuticals (22nd and 21st). The Brazilian pharmaceutical market is the 8th biggest in invoice spending, with growth led by low-cost medicines but expected to expand to high-cost products. While the Brazilian government is the 14th biggest in health expenditure, given the Unified Health System (SUS), it is much less prominent in terms of the share of the GDP (74th), per capita (77th), or share of health expenditure (123rd).

Table 1.2. Summary of socioeconomic and innovation statistics about Brazil

Statistic	Value	Rank	Year	Source
Population (million)	216.4	7	2023	World Bank (2024)
GDP, PPP$ (billion)	2,173	7		
GDP per capita, PPP$	20,584	86		
Human Development Index	0.760	89	2022	UNDP (2024)
Overall loss in Human Development Index due to inequality (%)	24.1	63		
Global Innovation Index	-	50	2024	WIPO (2024b)
Patent applications published by the INPI	25,025	10	2022	WIPO (2024c)
Patent applications filed by Brazilians anywhere	6,602	23		
Pharmaceutical patent applications published by the INPI	3,001	9		
Pharmaceutical patent applications filed by Brazilians anywhere	429	22		
Patents granted by the INPI	23,546	8		
Patents filed by Brazilians granted anywhere	3,502	25		
Pharmaceutical patents granted by the INPI	1,340	8		
Pharmaceutical patents filed by Brazilians granted anywhere	128	21		
Invoice pharmaceutical spending, $ (billion dollars)	36	8	2023	IQVIA (2024)
Government health expenditure, $ (billion dollars)	74.3	14	2021	WHO (2024a)
Government health expenditure per capita, PPP$	740.4	77		
Government's share of health expenditure (%)	45.5	123		
Government health expenditure over GDP (%)	4.5	74		

Brazil is a big developing country facing even bigger socioeconomic challenges. As one of the first to introduce patent legislation, it has always explored different designs for this policy. Historically, Brazil has been one of the leaders in the developing world's resistance to

the international push for stronger IPR regimes, especially for pharmaceuticals. Even in the 1990s, when Brazil reformed its IPR system and went beyond what the TRIPS Agreement had mandated in many aspects, it still enjoyed some flexibilities for pharmaceuticals. These factors make it an excellent case for analysing the importance of how pharmaceutical patent policies are implemented in developing countries.

1.4 Research questions, empirical strategy and main findings

This thesis aims to draw lessons from the implementation of pharmaceutical patenting in Brazil after the country signed the TRIPS Agreement about its novel policies that explore the flexibilities under TRIPS, given the recommendation that the country invests in strengthening the examination by the patent office as a preventive measure to promote balance in the patent stimuli. The aim is not to question if the current pharmaceutical patent system is fit for purpose from the perspective of developmental challenges and access to drugs, but rather to take a pragmatic approach: investigating how to promote balance in the patent system without changing its core institutions, like the TRIPS Agreement. Furthermore, the thesis tries to fill the gap in the literature on empirical analyses of TRIPS flexibilities in developing countries. These policies have been proposed for decades (Musungu and Oh 2006; Deere 2009; Correa 2014; 2022; Oswald and Burri 2021), but there is little evidence about their implementation and effects (Sampat and Shadlen 2015; 2017; 2018; t' Hoen et al. 2018; Sarnoff 2020; Tenni et al. 2022).

The main research question of this thesis is: What lessons can be drawn from the implementation of pharmaceutical patenting in Brazil after the TRIPS Agreement about the flexibilities to design patent policies that strengthen examination? In addition, this thesis has three subsidiary questions, one for each of the case studies from which lessons are drawn.

The first subsidiary question is: How has the Backlog Reduction Plan affected the grant rate and the duration of examination and overall prosecution at the INPI? This question is answered in Chapter 2, with an analysis inspired by the policies recently introduced by the INPI to tackle the historically high backlog of applications pending a decision. Assuming that examination was slow, the INPI started adopting reports published by other offices for applications covering the same inventions. Expecting this to expedite the prosecution significantly, the INPI also increased examiner productivity targets. This chapter investigates

the effects of using another office's reports and increasing productivity targets on the likelihood of applications being granted and the average periods of substantive examination and overall prosecution (from filing to a decision). The analysis includes 53,597 pharmaceutical applications filed at the INPI from 1995 and decided by 2022. Considering applications covering the same inventions in each jurisdiction, it also compares grant rates from the INPI and 14 other offices: Argentina, Australia, Canada, China, Colombia, the European Patent Office (EPO), Israel, Japan, the Republic of Korea, Mexico, Peru, Russia, the United States, and Uruguay.

The results show that the INPI is on a trajectory of granting more often and making fewer objections before granting. This increase in grant rate is bigger than the international average. The Plan influenced these changes, especially by forcing examiners to use another office's report. The INPI examiners were already efficient, and examination has become slower under the Plan. Apart from an initial wave of abandonments, the Plan has had a limited effect on the backlog. Thus, it has more effectively led examiners to grant more often and with fewer objections than expedited the prosecution. This suggests a possible drop in examination rigour, which should be tested in future studies. Based on the empirical literature on similar policies, these results are expected given how the Plan was designed and implemented. Thus, the INPI should replace the Plan with policies that strengthen and expand examination capacity to become as efficient as its examiners.

The second subsidiary question is: What contributions can health regulators offer to the scrutiny in pharmaceutical patent examination when applications must be examined by the regulators and the patent offices, considering the patentability criteria cited as grounds for negative decisions? Chapter 3 answers this question by analysing one of the TRIPS flexibilities introduced by Brazil: the dual examination of pharmaceutical patent applications by the INPI and Anvisa from 2001 to 2021. Both entities considered the same patentability criteria when examining pharmaceutical applications, but this chapter investigates if they thought specific articles were more relevant and if one influenced the other one over time. For that, the analysis involved reading 2,589 negative decisions to estimate how often each entity cited the different articles of the LPI and assess if the views adopted tend to be complementary or redundant.

One of the main findings is that the INPI initially focused on traditional patentability – novelty, inventiveness, and industrial applicability – while Anvisa had a more diverse approach and cited invention description most often. Despite the conflictual relationship leading to

frequent disagreements, the entities converged to higher patenting standards, with more patentability criteria considered relevant grounds for rejecting an application. The most significant shift was for the INPI, whose decisions became closer to Anvisa's than its own from previous years, especially regarding invention description. Giving higher relevance to this aspect is consistent with the goal of promoting balance in the private and public stimuli in patenting. Therefore, the stability and enforcement of the dual examination system were strengthened by having clearer and more limited rules, which made it not just non-redundant but complementary, and having the two entities became almost symbiotic or mutually nutritious. Still, the lack of clarity about the shared responsibilities and intense legal, bureaucratic and political debates that ensued have made implementing this multi-entity policy even more complex. Thus, this analysis provides lessons to Brazil and other countries that may wish to implement similar policies about Anvisa's role in increasing patent examination rigour.

The third subsidiary question is: How does the interaction between patent exclusivity and therapeutic substitutability influence the competition in centralised public tenders for HCV drugs? To answer this, Chapter 4 connects the microcosmos of the patent office with the drug market, investigating the broader influences of the policies analysed in the previous chapters by looking at the history of centralised public procurement of HCV drugs by the Brazilian Ministry of Health (MoH) as a strategy to reduce drug prices and promote access. This case study includes four analyses: identifying which regimens were recommended since 2015 and how they differed in effectiveness; identifying the products with marketing approval to determine which versions were available; mapping the patent landscape for all drugs to understand the role of patent examination and opposition in determining the level of protection; and examining the public procurement history to analyse how the manufacturers and the government negotiated, focusing on tenders.

This chapter finds that the government could induce competition by having manufacturers of reference drugs compete among themselves and with generic producers, which was possible because of two factors. First, the fact that the recommended treatments had the same therapeutic effectiveness led to direct competition among all alternative treatments, even if under patent protection. Second, the production of generics was enabled by strong patent examination measures, a refusal to let pending applications produce *de facto* exclusivity, and originators' commercial strategies. To discuss the results, this chapter includes a matrix of four competition scenarios based on the level of patent exclusivity and therapeutic

substitutability and draws from the literature on patent protection, drug prices, and pharmaceutical tendering. This case study illustrates the potential benefits and shortcomings of inducing competition. It also shows how the dual examination system was one of the effective preventive measures that Brazil had in place to promote patent examination rigour, and how the Backlog Reduction Plan has led to much higher grant rates, challenging the strength of examination. Lastly, while technology transfer policies for local production helped this strategy of inducing competition, price regulation played no role in centralised procurement.

The remainder of this thesis is divided into four chapters. The first three present the analyses described above. The logical sequence starts with an analysis of pharmaceutical patent examination speed and grant rates. Then, an investigation of how the dual examination mechanism affects the grounds for negative decisions. Next, with a study of the effects of patent exclusivity and therapeutic substitutability on competition among patented and generic drugs, highlighting the ole of the policies studied in the two previous chapters. Finally, Chapter 5 discusses the main contributions of this thesis to policy design and the empirical literature, explains the limitations of the case studies, and presents the concluding remarks.

2 THE BRAZILIAN STRATEGY OF SIMPLIFYING PATENT EXAMINATION TO EXPEDITE PROSECUTION

Since the introduction of pharmaceutical patenting in developing countries in the 1990s, many scholars have emphasised the importance of rigorous examination (Correa 2000; Drahos 2008; 2010; Shadlen 2013; 2017; Sampat and Shadlen 2015). It is argued that lax examination and the subsequent granting of low-quality patents can have worrying consequences for public health by unduly extending exclusivity which may stifle competition and restrict access and affordability. Although more evident in the pharmaceutical sector, this is an issue for all patents. Economically, patents are designed to produce a balanced system of incentives for innovation that rewards the patentee with exclusivity in exchange for knowledge disclosure (Macdonald 2002; Granstrand 2005; Andersen 2006; Rockett 2010). Thus, lax examination may lead to the overprotection of innovation by tipping the balance in favour of the inventor. Considering the importance of promoting balanced patent stimuli, this chapter investigates how a recent policy introduced by Brazil affects the duration and the outcome of pharmaceutical patent prosecution.

The challenge of ensuring the rigorous examination of patent applications is even trickier in developing countries, whose patent offices typically face bigger resource constraints: more precarious infrastructure and fewer and more overburdened examiners. In addition, there is less regulatory capacity to mitigate the effects of lax examination due to asymmetries in access to the judicial system and negotiation powers, especially when national competitors litigate patents owned by (larger and typically more resourced) transnational companies. For pharmaceuticals, it is also the case that health-related socioeconomic challenges are more pressing while national industries are less developed. Thus, some scholars propose that developing countries should focus on rigorous examination to prevent overprotecting innovation, while developed countries may rely on post-grant corrective measures, like administrative appeals or litigation (Correa 2000; Drahos 2008; 2010; Shadlen 2013; 2017; Sampat and Shadlen 2015; Frakes and Wasserman 2023).

Despite these concerns being raised for decades, there have been few large-sample empirical analyses of patent prosecution in developing countries (Tong et al. 2018; Abinader 2020; de Rassenfosse et al. 2021; Zhu et al. 2022; Yang et al. 2024). This thesis is the first to do so for pharmaceutical patents in Brazil since previous studies had smaller samples (Shadlen 2011; 2017; Sampat and Shadlen 2015; 2017; Mercadante and Paranhos 2022).

The empirical focus of this chapter is a set of measures introduced in 2018 to reduce the backlog of pending applications. At the INPI, as in most patent offices that examine applications instead of simply registering them, the same examiner is responsible for first producing the prior art search report which lists the patent and non-patent documents considered relevant to determining the novelty and inventiveness of applications and then conducting the substantive examination of these and all other patentability criteria (Drahos 2010). However, the INPI has been experimenting since 2018 with importing prior art search reports published by other offices for twin[4] applications via the Backlog Reduction Plan (INPI 2024a). Assuming this would reduce the examination workload, the INPI also made examiners decide faster by increasing productivity targets. Thus, the Plan aims to simplify examination to expedite prosecution and, as a result, reduce the backlog.

In that sense, the Plan is a good case study of the trade-off between examination speed and grant rates, advancing the debates on adopting someone else's prior art searches (Lemley and Sampat 2012; Cotropia et al. 2013; Lei and Wright 2017; Yamauchi and Nagaoka 2015; Kim and Oh 2017; Latsch 2018) and on forcing examiners to decide faster (Harhoff and Wagner 2009; Frakes and Wasserman 2017; 2023; Kim and Oh 2017; Marco et al. 2019; Nagaoka and Yamauchi 2022). This chapter analysed 53,597 pharmaceutical applications filed in Brazil from 1995 that reached an outcome by 2022. First, it investigated how the Plan influenced the duration of prosecution and substantive examination. Next, it estimated the influence on the likelihood of applications being granted and granted without any objection from the examiner. Finally, it contrasted grant rates for the INPI and fourteen other offices.

While the Plan has sped up prosecution, this was mostly by anticipating the start of the examination. The Plan prolonged the examination period, which might signal it made this task more complex. Moreover, the results show a reversal of the historical tendency of low grant rates for pharmaceutical applications. This growth in grant rates is directly related to the Plan, which has led examiners to grant patents more often and make fewer objections before granting. Considering twin applications, this growth was more significant than in other offices. These findings suggest a drop in examination rigour in Brazil, which should be confirmed in future studies that compare the quality of patents granted under and outside the Plan.

[4] Applicants must file in each country where they seek protection, with each application being called a 'twin' and the collective a 'family'. Twins may not be identical due to the differences in patenting criteria and examination guidelines. There can be multiple twins in a country, given filing strategies and divisional applications.

This chapter also argues that the Plan is flawed by design for assuming that Brazilian examiners were inefficient. On the contrary, their efficiency was comparable to that of some of the biggest patent offices, and the prosecution was delayed by the workload imbalance, not by slow examination. Comparing the results with the empirical literature on patent examination and other experiences of adopting someone else's prior art searches and forcing an increase in productivity, the Plan has been more effective in increasing grant rates than accelerating the prosecution. Thus, this policy should be reevaluated, given the potentially harmful consequences of a drop in examination rigour.

The remainder of this chapter consists of seven sections. First, a brief literature review on the trade-off between patent examination speed and grant rates. Then, a detailed explanation of the Backlog Reduction Plan. The Methodology presents the data challenges, the empirical strategy and some descriptive statistics. The next two sections present the results and compare production statistics from the INPI and other offices. Then, the Discussion analyses the findings based on the empirical literature. Finally, the Conclusion and recommendations.

2.1 The trade-off between patent prosecution speed and grant rates

Any patent office that examines applications instead of simply registering them will face a challenge in managing the backlog of pending applications. This section summarises the empirical literature on policies that aim to expedite prosecution, their effects on the grant rates, and the implications for examination rigour and patent quality.

Drahos (2010) reported that Japan introduced the outsourcing of search reports in 1989 and Korea followed suit in 1996. Less than half of search reports are done by each office's own examiners (Yamauchi and Nagaoka 2015; Kim and Oh 2017). Given the costs of outsourcing,[5] examiners have a fixed number of search reports that they may choose to outsource, leading to this happening more often for less complex inventions (Yamauchi and Nagaoka 2015). This makes sense given examiners' capacity to identify low-quality applications and manage their workload (Lei and Wright 2017). Since how much examiners benefit from someone else's work is contingent on how similar the guidelines are (Drahos 2010), the offices from Japan and Korea hire third-party searchers to produce search reports for some applications using each office's guidelines, preserving homogeneity across decisions. Apart from discussing the

[5] Outsourcing cost Japan 40% of direct expenses on examination in 2010 (Yamauchi and Nagaoka 2015).

outsourced report with the searchers, examiners are allowed to conduct further searches before following on with the substantive examination, especially in the periodic quality control analyses, which may lead to penalties for the searcher.

Yamauchi and Nagaoka (2015) praised outsourcing in Japan, arguing that it has led to faster prosecution, lower grant rates, and fewer appeals, but also said that this was contingent on outsourcing being restricted to low-quality applications. Similarly, Kim and Oh (2017) found that the Korean policy reduced the likelihood of grants and led to fewer and less frequently successful appeals. They argue that a crucial aspect of this policy is that both offices implemented outsourcing to reduce the workload pressure on examiners, allowing them to dedicate more time to examination, especially for more complex inventions.

However, some oppose outsourcing search reports altogether. Cotropia et al. (2013) showed that examiners rarely consider prior art submitted by applicants. It might also be that examiners are less convinced about findings from another examiner. If forbidden from or incapable of allocating time to further searches, examiners might become biased to grant. Based on interviews with examiners from several offices, Drahos (2010) reported that they usually acquire vital knowledge for the examination by searching for the prior art. Thus, basing the examination on someone else's work might be disadvantageous from a productivity perspective, apart from potentially affecting patent quality. If outsourcing is an alternative to hiring more examiners, this might also have a pro-grant bias by increasing the average seniority of the office. Lemley and Sampat (2012) found that more senior examiners grant more often, cite fewer documents in prior art reports, and restrict the patent scope less often.

Turning to policies that increase the pressure on examiners to decide faster, Kim and Oh (2017, p. 1015) argue that this restricts the examiners' capacity to conduct appropriate prior art research, affecting the level of scrutiny in the examination. As a result, examiners grant more often, cite fewer references, and make fewer rejections based on inventiveness, and the twins of these patents with faster grants are less frequently granted by other offices, suggesting lower patent quality (Frakes and Wasserman 2017). Similarly, Marco et al. (2019) found a link between faster examinations and patents being granted with broader scope. For pharmaceutical patents on incremental or secondary inventions, Frakes and Wasserman (2023) suggest that spending extra resources to allow examiners enough time to make decisions may not only avoid reducing patent quality but also effectively reduce litigation costs and generate innovative

gains, with generics entering the market earlier. There is also the question of how efficient examination can be before the office becomes a rubber stamp.

Lastly, some have investigated the potential benefits of some delay in prosecution. Nagaoka and Yamauchi (2022) analysed the reduction in Japan of the deadline for examination requests from seven to three years, concluding that it increased information constraints, which affected the examination and lowered the quality of patents being granted. Thus, there are limits to the gains in anticipating the start of the examination. Neither does it seem to be the case that applicants themselves always want prosecution to be as fast as possible. Harhoff and Wagner (2009) suggested that applicants tend to accelerate prosecution if grants are likely and to delay when they expect a negative outcome. Nonetheless, applicants may still find delaying grants interesting financially to delay paying higher fees or strategically to prolong uncertainty for competitors, especially for technological sectors with long innovation cycles like pharmaceuticals. Looking at pharmaceutical applications in China, Zhu et al. (2022, p. 14) suggested applicants could strategically delay prosecution by 'having a complicated application that involves many different technological elements, or that introduces complex, ambiguous or irrelevant information to confuse examiners'. Likewise, Mercadante et al. (2018) found applicants contributed to delaying the prosecution of pharmaceuticals in Brazil.

The empirical literature on policies that expedite prosecution has identified negative consequences for patent quality when examiners cannot dedicate enough time to each application. Some have found that outsourcing prior art searches can strengthen examination if designed to allow examiners to dedicate more time to more complex applications and the outsourced work has the same standard and follows the same guidelines. However, others have argued that outsourcing this task compromises an essential aspect of examination, producing negative consequences. Some delay in prosecution might also be beneficial to examiners by reducing information constraints and to applicants for financial and strategic reasons.

2.2 The Backlog Reduction Plan

Brazil excluded pharmaceutical products and processes from patenting in Brazil in 1945 and 1969, respectively. With the enactment of the LPI in 1996, it reintroduced pharmaceutical patenting as mandated by the TRIPS Agreement. Signed in 1994, TRIPS required countries to accept patent filings from any technical field from 1995 but allowed middle-income countries

that had been excluding pharmaceuticals to only begin prosecuting these applications in 2005. However, Brazil started doing it already in 1997, posing a challenge to the patent office, the INPI, since it did not have enough time to hire and train new examiners. This only deepened the historical backlog of pending applications, which is still an issue in Brazil: there were 115,414 pending applications in February 2024 considering all technical fields (INPI 2024b).

The INPI has explored different strategies to improve examination capacity. In 2000, it tried to hire temporary examiners, but the Supreme Court ruled examination could only be done by civil servants hired on permanent contracts by the INPI (Garcez Júnior and Moreira 2017). The INPI has also tried to partner with the National Council for Scientific and Technological Development (CNPq) to train and hire external researchers to assist in the examination (INPI 2018a). Anvisa was called upon to assist in the examination of pharmaceutical inventions. From 2001 to 2021, the INPI could only grant patents related to products for human health if Anvisa also gave consent, leading to much conflict between them (Sampat and Shadlen 2017; Shadlen 2017; Mercadante and Paranhos 2022).

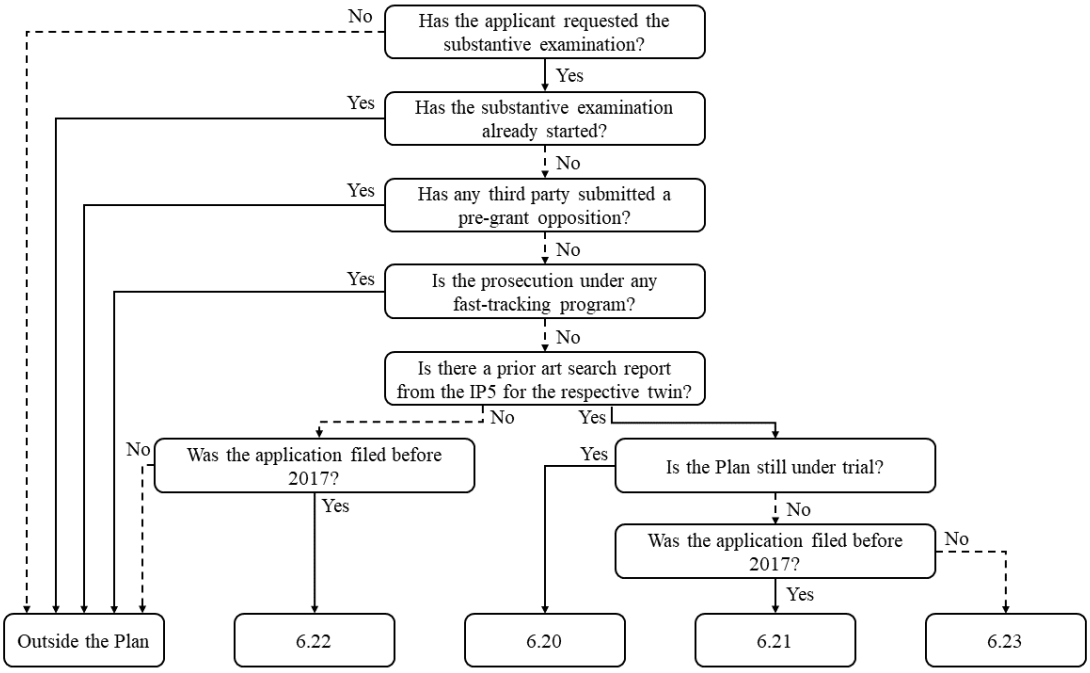
The most controversial policy Brazil has proposed to deal with the backlog was granting every pending application except for pharmaceuticals, as announced in the Public Consultation nº 2 of 2017 (INPI 2024c). This is the opposite of what the literature recommends since, instead of investing in the examination as a preventive measure, Brazil would rely on court decisions to cancel all unduly granted patents. This proposal was abandoned after an overwhelmingly negative reaction based on the fear of the negative consequences of overprotection and legal uncertainty. It would also just transfer the problem from the INPI to the judicial system, which had a backlog of 79.5 million pending lawsuits in 2017 (CNJ 2024).

After that proposal failed, the INPI introduced another prosecution-expediting policy, but this time without any public consultation. In 2018, it began structuring what was later called the Backlog Reduction Plan (INPI 2024a). The Plan has had four versions, defined by the different office actions (OAs) that govern it. The INPI publishes these as *despachos* in the Industrial Property Gazette to, among other things, request explanations or changes and to communicate its preliminary opinions or final decisions. An application is placed ‘under the Plan’ when the INPI publishes an OA 6.20, 6.21, 6.22 or 6.23.

Figure 2.1 summarises the selection process for prosecution outside or under a version of the Plan. The first step is placing outside the Plan any application: a) whose applicant has

not requested the substantive examination; b) already under examination; c) that has received a pre-grant opposition (PGO); or d) under fast-tracking.

Figure 2.1. The allocation process for the Backlog Reduction Plan



Next, the INPI searches for prior art search reports on twin applications in the Common Citation Document (CCD) database from the five biggest patent offices (IP5): China, the EPO, Japan, the Republic of Korea, and the United States (INPI 2019a; IP5 2024a). If no report is found and the application was filed after 2016, the prosecution continues outside the Plan. If there was no report and the application was filed before 2017, the INPI publishes OA 6.22 (INPI 2019b).[6] If the INPI found a report during the trial period, it would publish OA 6.20 regardless of the filing year (INPI 2018b). Lastly, the INPI publishes the imported reports in OA 6.21 for applications filed before 2017 (INPI 2019c; 2021a) or OA 6.23 for those filed after 2016 (INPI 2021b; 2022).

The INPI expected examiners to decide faster if they did not have to do the prior art search themselves. Thus, it increased the examiners' productivity targets, measured by publications of search reports, substantive requests, preliminary opinions and final decisions (INPI 2019d; 2021c; 2023a). The INPI pressured them to make faster decisions by reducing how many production points were awarded per type of publication. In that sense, the INPI

[6] Although not declared explicitly by the INPI, examiners explained that OA 6.22 was created to extend the Plan to applications filed by Brazilians, who are less likely to file elsewhere; hence, there is no report to import.

increased productivity targets when examiners used imported reports (OA 6.21 or 6.23).[7] Paradoxically, it also increased the targets for prosecution under OA 6.22 despite examiners still producing their own reports.[8]

As a result, there are different types of prosecution at the INPI, based on the two treatments of the Plan. Prosecution outside the Plan had no treatment. Prosecution under OA 6.20 only had imported reports. Prosecution under 6.22 only had higher productivity targets. And prosecution under 6.21 or 6.23 had both treatments. In Table 2.1, I summarise the differences in prosecution when outside or under the Plan.

Table 2.1. Summary of the standard prosecution and the four versions of the Plan

Characteristic	**Outside the Plan**	**6.20**	**6.21**	**6.22**	**6.23**
Search report	INPI's own	Imported	Imported	INPI's own	Imported
Productivity targets	Normal	Normal	Increased	Increased	Increased before June 2023, then normal
Additional searches	Allowed	Allowed	Forbidden before November 2021, then allowed	Forbidden before December 2020, then allowed if the report was done using an automated system, and for all other cases from November 2021	Forbidden before November 2021, then allowed
Description sufficiency	Must consider	Allowed to ignore if signalled in the imported report	Allowed to ignore if signalled in the imported report	Must consider	Allowed to ignore if signalled in the imported report
Period	–	10/2018-07/2019	07/2019-	07/2019-	04/2021-

After the trial period, the INPI initially prohibited examiners from conducting further searches, limiting the examination to the documents and relevance indicated by the original examiner for assessing novelty and inventiveness. Although the INPI examiners produced their own reports under OA 6.22, further searches were also forbidden.[9] From December 2020, these searches became allowed if the report was done with an automated system (INPI 2020). However, examiner associations obtained an injunction in November 2021 that allowed further searches in any prosecution, as part of an ongoing lawsuit against the Plan (AFINPI 2021).

The last change introduced by the Plan allowed examiners not to assess if inventions were sufficiently described if this issue had not been cited in the imported report (INPI 2029b). The LPI determines that the application document should describe the invention object clearly

[7] From April 2021 to June 2023, productivity targets under 6.23 were higher than outside but lower than under 6.21 or 6.22. Since then, targets have been brought down to normal levels, leaving only the importation of reports.
[8] While the search report awarded normal production points, subsequent publications awarded fewer points.
[9] This might explain why their production points were also reduced.

and sufficiently enough for a person with average knowledge to reproduce it and that the claims should be clearly and precisely defined and based on the descriptive report. Since no report is imported under OA 6.22, examiners are not allowed to ignore this (INPI 2019d).

Finally, the OAs present the imported report (OA 6.20, 6.21, or 6.23) or the INPI examiner's own report (6.22) and request that applicants reply and make any necessary changes to the application, which is an extra step in the prosecution. They do not include an opinion on the patentability of the invention, which is published later. Still, applicants might get a sense from the listed prior art if the examiners are likely to find issues with the novelty or inventiveness of the invention, for example. This could lead applicants to abandon the applications. Applicants have different deadlines to reply to the Plan's OAs, depending on the version (INPI 2018b; 2019c; 2019d; 2021a; 2021b; 2022). Applications are considered abandoned if the applicants fail to reply.

In that sense, the Backlog Reduction Plan is an attempt from the INPI to tackle the chronically high backlog of pending applications by importing prior art search reports from the IP5 and forcing Brazilian examiners to work faster. Considering these two treatments, the Plan has created four groups of applications: untreated, under just imported reports or higher productivity targets, or under both. It also introduced a new obligation to applicants, leading to the end of prosecution if ignored. The next section explains how this chapter investigates if the Plan reaches its goals of speeding up examination and the consequences for rigour.

2.3 Methodology

This section presents the data selection and management challenges, the three-part empirical strategy to investigate the Backlog Reduction Plan considering the trade-off between patent examination speed and rigour, and some descriptive statistics.

2.3.1 Data

All data for this analysis were extracted from the Spring 2023 Edition of the EPO's PATSTAT database which aggregates data shared by patent offices (EPO 2024a). This investigation focused on filings in Brazil, except for those under nine categories: a) other types

of applications, like utility models and certificates of addition; b) artificial applications;[10] c) duplicates; d) pipeline patents;[11] e) those with International Patent Classification (IPC) codes missing; f) those with legal event data missing; g) those with unclear prosecution histories;[12] h) those filed before 1995; or i) those pending by the end of 2022.

The IPC codes were used to identify 53,597 pharmaceutical applications.[13] Thus, the sample includes 53,597 pharmaceutical applications, representing 71.2% of the universe of pharmaceutical invention patent applications reported on PATSTAT as filed in Brazil since the TRIPS Agreement. The rest were either pending by the end of 2022 (27.1%) or had missing or unclear data (1.7%). Thus, the sample comprises 97.7% of pharmaceutical invention patent applications filed from 1995 and with a decision by 2022.

Next, five prosecution aspects were identified from each application in the sample: a) the filing date; b) the date of the first substantive OA, marking the beginning of substantive examination;[14] c) if the application was pending by the end of 2022; d) the outcome – granted, rejected, or abandoned – and outcome date; and e) if and when it was placed under the Plan.

As explained in Section 2.2, the two main effects of the Backlog Reduction Plan were importing prior art search reports published by the IP5 offices and making examiners decide faster by increasing productivity targets. However, the Plan also forbade examiners from conducting further searches and authorised them to ignore the analysis of description sufficiency, depending on the version of the Plan and when the examination happened. Unfortunately, this chapter could not directly investigate the prohibition of further searches or

[10] PATSTAT creates artificial applications when an application references another that is not listed in the database.
[11] This mechanism allowed applicants to file older applications that could not have been filed before because Brazil used to exclude them from patenting, like pharmaceuticals. Pipeline patents were issued without examination for a 20-year term from the priority date if the original application had been granted, the invention had not been introduced in any market, and there were no significant efforts to develop it in Brazil.
[12] Including these applications would require manually reading the individual prosecution histories, breaking the methodological consistency of this analysis.
[13] Since applications normally have multiple IPC codes, the same application may be classified as belonging to multiple categories, e.g. pharmaceutical and chemical, but it might be more relevant to one than the other. Using the weighted concordance between IPC codes and the 2nd Revision of the Statistical Classification of Economic Activities (NACE) developed by Eurostat (2015) and incorporated by PATSTAT, this chapter considers pharmaceutical applications are those with the code IPC A61K (except A61K 8/*) or with that code associated to A61P, C07D, C07H, C07J, C07K, C12, C12P, or C12Q, as long as applications are at least 75% pharmaceutical. Therefore, this analysis is focused on applications that are primarily pharmaceutical.
[14] Considering OAs containing the report under the Plan (6.20, 6.21, 6.22, 6.23), requests for substantive changes or explanations (6.1), the intention to reject the application (7.1), or the decision to grant (9.1) or reject (9.2).

the authorisation to ignore description sufficiency because this would require information that is not included in PATSTAT and might not be publicly available anywhere.[15]

Therefore, the analysis of the Plan was restricted to two treatments: *Imported Reports* and *Higher Targets*. Thus, the sample was separated into two control and three treated subsamples. The control subsamples included decisions outside the Plan before or after it was introduced. The treated subsamples include decisions under *Imported Reports* only (under OA 6.20), under *Higher Targets* only (6.22), or both (6.21 or 6.23).[16]

2.3.2 Prosecution and Examination Lags

The first part of the empirical strategy was to analyse how the Plan influenced the length of the examination and overall prosecution. To do that, this analysis estimated two periods that ended on the outcome date: the *Prosecution Lag* starts on the filing date, and the *Examination Lag* starts on the date of the first substantive OA. Then, it compared the lags across the five subsamples: outside the Plan before the Plan period, outside the Plan in the Plan period, under *Imported Reports*, under *Higher Targets*, and under *Imported Reports* and *Higher Targets*.

The standard methodology for WIPO and many offices' reports is to measure the period from the substantive examination request to the outcome (IP5 2024b; WIPO 2024c). In Brazil, applicants must request this within three years from the filing date. Although Mercadante et al. (2018) have found that pharmaceutical applicants tend to wait until the last days to do so, this period can be a lot shorter, especially when applications are fast-tracked. Unfortunately, PATSTAT does not have any data on examination request dates, so anyone comparing this investigation with other studies should consider the different methodologies and the fact that the *Examination Lag* does not include the work preparing the first substantive OA.

Another limitation of this analysis is that it cannot distinguish between fast-tracked prosecutions and those that had to wait in the backlog pile. Until July 2019, the INPI reported to PATSTAT when fast-tracking was requested, denied or granted, but the OAs did not inform the specific fast-tracking programme. After the INPI introduced new OAs for each programme,

[15] For example, if an automated system was used for the report in OA 6.22 or if imported reports listed description sufficiency. There is also a compliance issue. In interviews for this thesis, examiners said they often cited other relevant documents they already knew from previous cases, escaping the prohibition of further searches.
[16] Since the data includes outcomes by 2022, prosecutions under 6.23 were still under *Higher targets*.

it stopped reporting this legal event altogether, as confirmed by PATSTAT's summary of legal event data coverage (INPI 2019e; EPO 2024b).

In addition, several applications should have been declared abandoned, but the INPI has yet to publish this outcome. These were coded as pending and excluded from the sample. Similarly, many applications were only declared abandoned more than a decade after what had triggered this outcome. Although these late publications indicate the correct abandonment date, PATSTAT only includes the date of the late publication, not the correct outcome date. Estimating the lags for all outcomes, including abandonments, would bias the analysis. This study focuses on how the Plan affected the normal examination course, whereas abandonments can happen for unrelated reasons such as a change in applicants' strategies). Thus, the analysis of lags focused on examiner decisions: grants and rejections.[17]

2.3.3 Grants and Direct Grants

The second analysis employed ordinary least squares (OLS) regressions using time-invariant variables and robust standard errors to investigate the Plan's effect on the outcomes,[18] running separate regressions for the two dependent variables: *Grant* indicates if applications were granted, while *Direct Grant* captures those granted without examiner objections.[19] Knowing if examiners made any objection or if patents were granted exactly as filed demonstrates the examiner's influence on patent scope and serves as an indicator of scrutiny (Lemley and Sampat 2012). This should compensate for not reading the patent documents to identify changes to the text during the prosecution (Marco et al. 2019) or what share of the prior art cited in the final patent document was listed by the applicant voluntarily or was included by request of the examiner (Lemley and Sampat 2012; Frakes and Wasserman 2017).

The independent variables are *Imported reports*, *Higher targets*, and their combination, capturing the treatment effects versus prosecution outside the Plan. The regressions were repeated for all decisions and just those since the Plan was introduced to identify any

[17] When applicants fail to reply to substantive requests (OA 6.1), the INPI declares the applications substantively abandoned (*arquivamento técnico*), considering this an examiner decision (INPI 2023c). However, what triggered the outcome was the applicants' inaction, not a decision from the examiner. The publication of substantive requests instead of negative opinions (7.1) precisely means the examiners have not yet decided. Thus, this thesis does not follow the INPI in considering these abandonments examiner decisions.

[18] Although the introduction of the Plan is an exogenous shock, there are multiple versions of the Plan that were introduced at different moments in time. In that sense, OLS regressions were chosen instead of a mixed cross-section difference-in-difference like Yang et al. (2024).

[19] The only OAs considered were 6.1 and 7.1 because these indicate substantive issues to be resolved.

generalised change to the likelihood of *Grant* and *Direct grant* that also affects decisions outside the Plan. They were also repeated for all outcomes and just examiner decisions to remove the influence of the applicants' propensity to abandon. In total, this led to eight regressions for each dependent variable.

Lastly, three control variables were used: *Filing year* fixed effects addressed right-hand censoring; *Outcome year* fixed effects dealt with changes in the guidelines or the number of patent examiners; and *Family size* controlled for invention importance by considering the number of twins in any country.[20] Since applicants tend to fight harder for inventions perceived as more important, these are expected to be granted more often (van Zeebroeck 2007; Harhoff and Wagner 2009; Kim and Oh 2017; Sampat and Shadlen 2017). Ideally, this analysis would also have controlled for fast-tracking since this is another indicator of invention importance (Harhoff and Wagner 2009; Yamauchi and Nagaoka 2015; Yang et al. 2024).

2.3.4 International grant rates

In the third analysis, applications were grouped by families the 53,597 applications with outcomes in Brazil were grouped according to the 52,349 direct families informed on PATSTAT. However, 3,436 families had no twin in any of the other offices. As a result, the sample for the international comparison of grant rates included 48,913 families.

The comparison of grant rates between Brazil and other offices required five methodological choices. First, granted families are those with at least one twin granted by that office. Second, pharmaceutical families are those with at least one Brazilian pharmaceutical twin. Third, 14 offices with legal event data on PASTAT were selected for the international comparison despite the differences in coverage: Argentina, Australia, Canada, China, Colombia, the EPO, Israel, Japan, the Republic of Korea, Mexico, Peru, Russia, the United States, and Uruguay (EPO 2024c). Fourth, PATSTAT's grant indicator was used for every office, including the INPI.[21] Fifth, there were two possible outcomes: grant or non-grant, not distinguishing between rejections, abandonments and pending applications.[22]

[20] Using PATSTAT's number of twins in the direct family, which is the closest way to select applications covering the same invention in different jurisdictions without reading each document (Martínez 2011).
[21] Comparing this method with the coding of legal event data, PATSTAT correctly indicated the family had at least one grant in 99.8% of cases for Brazil. This analysis assumed it should also be accurate for the other offices.
[22] The sample only contains applications with outcomes in Brazil, which is the slowest among these offices (Mercadante and Paranhos 2022). Thus, it is less likely that the twins are pending in other offices.

Based on these choices, grant rates were compared for pharmaceutical families examined by the INPI and another office. The analysis considered one other office at a time instead of all 14 to avoid reducing the sample to the 68 families examined by all.[23] Considering the 14 pairs, weighted average rates were estimated to compare Brazil with the international trend. The family-level grant rates should not be compared with the application-level results from the previous analysis given the methodological differences.[24]

Next, four subsamples were created: one with families whose twins were all decided outside the Plan; another under *Imported Reports* only; another under *Higher Targets* only; and another under both treatments. There was no separation between decisions outside the Plan before and after its introduction because more than half the families had both types. There were 10,977 families with twins under more than one version of the Plan, which were ignored to observe more uniform effects related to the Plan.

Since the Plan has no effect on the prosecution at other offices, this analysis assumes that the changes in grant rates in other offices reflect characteristics of the patent families that should also affect the prosecution in Brazil.[25] Therefore, a different variation in Brazil would indicate an effect of the Plan, and not something intrinsic to the families. Using the subsamples, the average grant rates in Brazil and each other office were estimated, comparing the difference between treated and control cohorts and subtracting the difference in Brazil from the international average. For example, if grant rates under *Imported Reports* were 10 percentage points (pp) higher than outside the Plan in Brazil and 4pp internationally, importing search reports would have comparatively decreased the quality of Brazilian patents because it increased the grant rate in Brazil more than internationally.

In synthesis, the international comparison of grant rates answers two questions: whether Brazil grants pharmaceutical applications more often than other offices, and if there were marginal changes to the Brazilian grant rates associated to the different Plan versions when controlling for intrinsic characteristics of the patent families.

[23] Comparing families shared by all offices would reduce the sample to only 68 families.
[24] Families may include non-pharmaceutical twins and were considered granted even if the only granted twin was non-pharmaceutical.
[25] Other studies have used the grant rate in other offices as a proxy for patent quality (Lemley and Sampat 2012; Frakes and Wasserman 2017; 2023).

2.3.5 Descriptive statistics

Table 2.2 presents descriptive statistics of the 53,597 pharmaceutical applications. Considering the entire analysis period, the *Grant* rate (18.4%) was higher than the rejection rate (14.7%), but most outcomes were abandonments (66.9%). Almost a quarter of applications that received a *Grant* had no examiner objection, as indicated by the *Direct Grant* rate (4.3%).

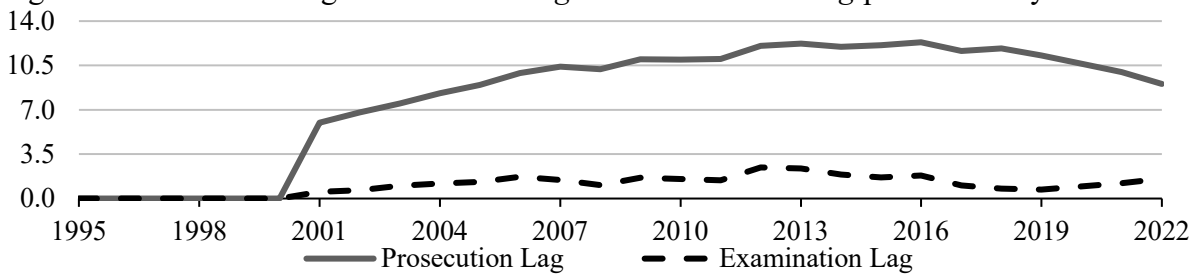
Table 2.2. Sample descriptive statistics

Variables	N	MEAN	SD	MIN	MAX
Grant	53,597	0.184	0.388	0	1
Direct Grant	53,597	0.043	0.203	0	1
Rejection	53,597	0.147	0.354	0	1
Abandonment	53,597	0.669	0.471	0	1
Family Size	53,597	18.430	13.987	1	290
Prosecution Lag	17,750	10.4	2.647	0.7	25.3
Examination Lag	17,750	1.3	1.114	0.0	14.0
Imported Reports	53,597	0.041	0.198	0	1
Higher Targets	53,597	0.013	0.114	0	1
Imported Reports & Higher Targets	53,597	0.133	0.339	0	1

Turning to invention importance, there is considerable variation in *Family Size*, with the average being 18 twins filed globally. The biggest family had 290 twins, which indicates it had multiple twins in some territories; in Brazil, there were two.[26] The most common family size had just one twin: 3,114 families, representing 5.9% of all pharmaceutical families.

The statistics related to lags have a smaller sample because, as explained in Subsection 2.3.2, they considered examiner decisions. Figure 2.2 presents the average lags per outcome year. It might be surprising that the shortest *Examination Lag* is zero, but that indicates this the first substantive OA was a grant, representing a case of *Direct Grant*.[27] While the mean examination takes 1.3 years, it has taken up to 14.0 years. Considering the entire *Prosecution Lag*, values range from 0.7 to 25.3 years, with an average of 10.4 years.[28]

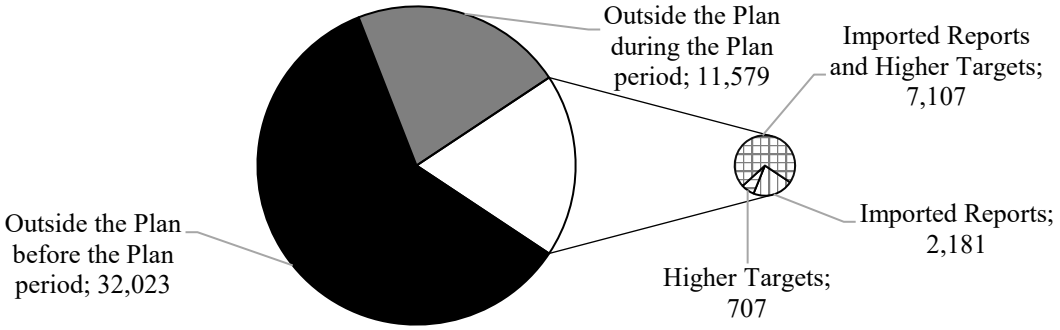
Figure 2.2. Annual average *Prosecution Lag* and *Examination Lag* per outcome year



[26] Families can have multiple twins in one country since applications can be split at filing or during the prosecution.
[27] It could not have been a rejection (OA 9.2) because the INPI must first publish an intention to reject (7.1).
[28] The fastest prosecutions might be cases of fast-tracking, but one cannot tell from PATSTAT's data.

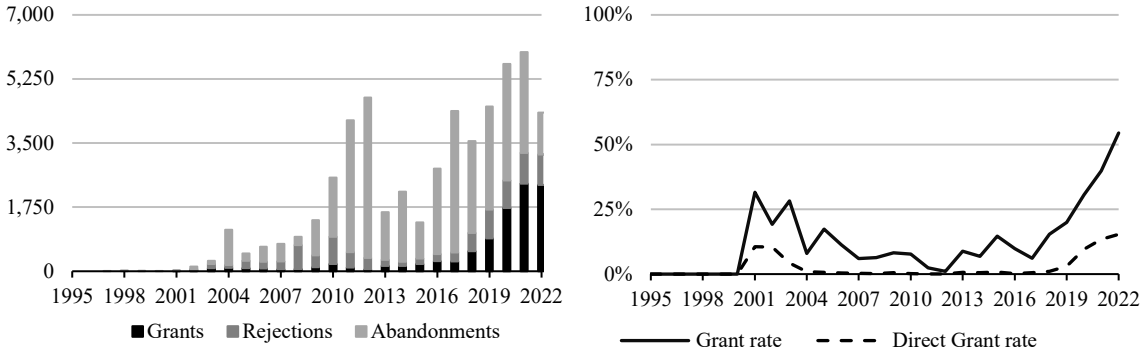
Overall, the Plan has accounted for 18.6% of outcomes and 34.5% of examiner decisions. Focusing on the Plan period, it accounted for 46.3% and 56.2%. Most of the Plan outcomes had *Imported Reports* and *Higher Targets* (71.1%), 21.8% only the former, and 7.0% only the latter. Figure 2.3 indicates the number of applications in the control and treated subsamples based on the Plan's two effects.

Figure 2.3. Number of applications in the five subsamples considering all outcomes and the entire analysis period



The INPI seems to be getting more productive even outside the Plan, since 40.3% of all outcomes happened in the four years of Plan period despite these applications being filed since 1995. Figure 2.4 shows that the number of annual decisions grew until 2020, led by abandonments and grants, followed by a drop due to fewer abandonments. As a result, the *Grant* rate grew continuously between 2017 and 2022 from 6.1% to 54.4% for all outcomes and 52.7% to 74.0% for examiner decisions. Although the INPI examiners have been granting more often than rejecting since 2014, *Grant* only surpassed 50% of annual outcomes in 2022. The share of *Grants* without any examiner objection also grew from 9.8% in 2017 to 28.1% in 2022. Considering all outcomes, *Direct Grants* went from 0.6% to 15.3%.

Figure 2.4. Number of outcomes, *Grant* rate and *Direct Grant* rate per outcome year



The next section evaluates what these changes meant for the *Prosecution Lag* and *Examination Lag*, the *Grant* and *Direct Grant* rates, and how Brazil compares to other offices in pharmaceutical patent examination.

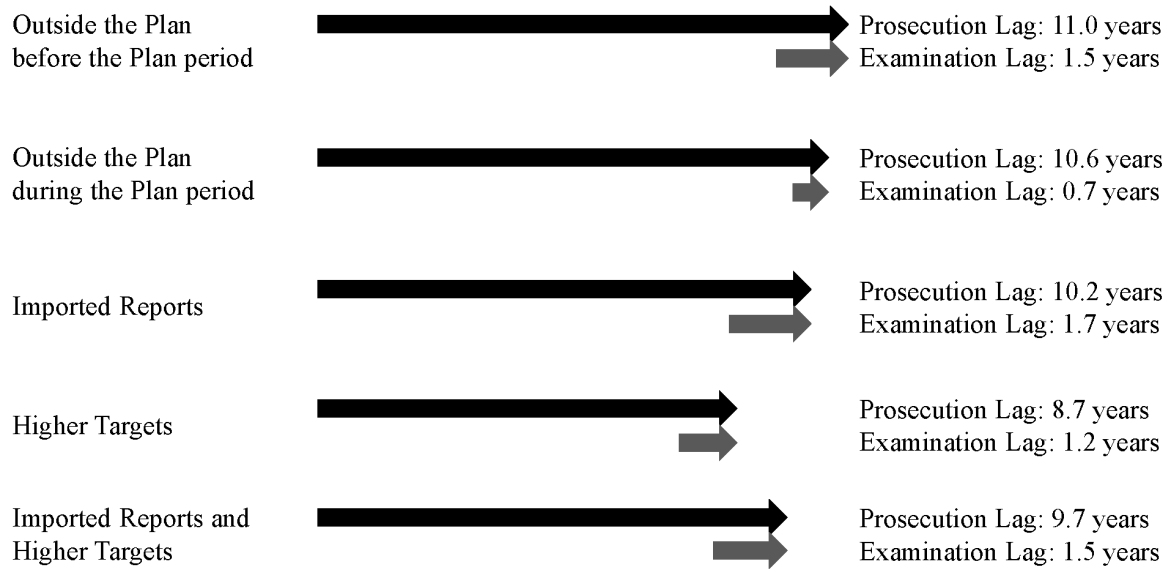
2.4 Results

This section presents the results of three analyses. First, it estimates how the Plan affected the *Prosecution Lag* and *Examination Lag* in Brazil. Next, it analyses the effects on the *Grant* and *Direct Grant* rates. Finally, it compares the outcome of patent prosecution of the same patent families in Brazil and 14 other offices.

2.4.1 How long do prosecution and examination take?

As explained in Subsection 2.3.2, the *Prosecution Lag* and the *Examination Lag* were estimated for examiner decisions to remove the bias from abandonments being published much later than the outcome date. Figure 2.5 contrasts the lags for decisions in the five subsamples.

Figure 2.5. Average *Prosecution Lag* and *Examination Lag* of examiner decisions



Looking only at the control subsamples of decisions outside the Plan, the *Prosecution Lag* and the *Examination Lag* are smaller in the Plan period than before. This suggests an overall acceleration of processes at the INPI that is more significant for examination. While some of these might be under fast-tracking, which excludes them from the Plan, 43.8% of examiner decisions in the Plan period were outside the Plan. It is unreasonable to expect that fast-tracking can affect the average so significantly.

Focusing on the *Prosecution Lag*, the Plan seems to be working well since all treated subsamples have shorter lags than the controls. The biggest acceleration of prosecution

happened for decisions under *Higher Targets* (1.9 years), while *Imported Reports* reduced it by 0.4 years and both treatments together reduced it by 0.9 years.

However, examination in the Plan period was faster outside the Plan, with *Imported Reports* alone causing the biggest delay. Some of this delay might come from an extra step under the Plan: applicants had to reply to the Plan's OAs before the examiner could continue examining. However, that does not explain why examiners took one year more, on average, to examine these applications than those outside the Plan. Another explanation is that examiners might have struggled to incorporate someone else's work, prepared using another office's guidelines and another country's patentability criteria.

It might seem odd for the Plan to delay examination but expedite prosecution. This is due to the examination starting earlier, as shown by the grey arrows in Figure 2.5, which might be explained by the INPI hiring new examiners in 2017 and the backlog being reduced (see Subsection 2.5). In the Plan period, the first substantive OA for applications decided outside the Plan was published after 9.9 years. Under the Plan, the publication happened after 8.5 years under *Imported Reports*, 7.5 years under *Higher Targets*, and 8.2 years under both. Comparing control subsamples before and in the Plan period, this period grew from 9.5 to 9.9 years.

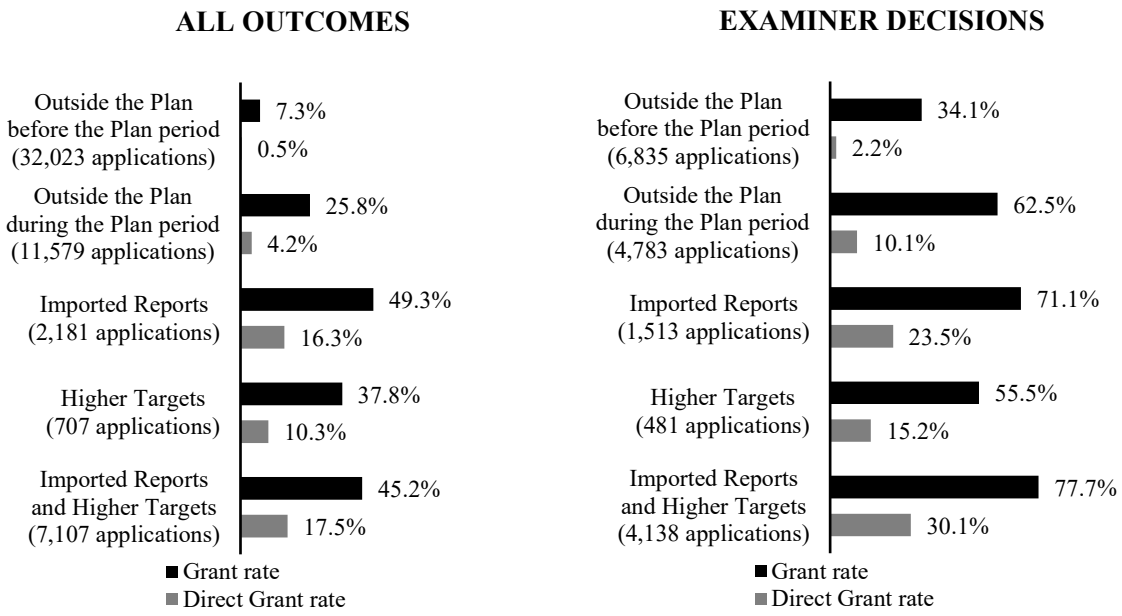
Therefore, while the Plan expedited prosecution by anticipating the start of examination, it made examination take longer, especially when examiners must base their analysis on another office's prior art search reports. Section 2.5 discusses these results by analysing the evolution of the INPI's backlog and comparing productivity and backlog statistics from the INPI and selected offices.

2.4.2 What drives the grant and direct grant rates?

To understand how the Plan affected all outcomes and examiner decisions, the *Grant* and the *Direct grant* rates were estimated for the five subsamples, as summarised in Figure 2.6. Comparing the control subsamples, both rates increased for prosecution in the Plan period. The treated subsamples had even higher rates. The combined effect of *Imported Reports* and *Higher Targets* led to the highest rates. The only exception was for *Grant* rates for all outcomes, which were higher under *Imported Reports* only. Some 77.7% of examiner decisions under both treatments were *Grants* and 30.1% were *Direct Grants*. Thus, this initial analysis suggests that the INPI has started granting more often and with fewer objections and importing reports seems

to have had a more significant effect than increasing the productivity targets. However, there is one odd result: the *Grant* rate for examiner decisions under *Higher Targets* was lower than the control in the Plan period.

Figure 2.6. *Grant* and *Direct grant* rates across control and treated subsamples of all outcomes and examiner decisions



To explain the rates and, especially, the odd result with examiner decisions under *Higher targets*, OLS regressions were run with the controls defined in Subsection 2.3.3. Considering all outcomes, Table 2.3 shows that *Grant* was 17.4pp more likely under *Imported reports* alone and 5.6pp more likely under both treatments. There was no significant effect under *Higher Target* alone. Focusing on examiner decisions, almost the same effect was found for the two treatments together (7.8pp), while the increase due to *Imported reports* became smaller (4.6pp), and *Higher targets* were associated with a significant decrease (-11.4pp). These regressions were repeated restricting the subsamples to applications with an outcome in the Plan period, finding almost the same effects. The only important difference was that *Higher Targets* alone led to a significant increase for all outcomes (5.1pp).

Therefore, the likelihood of *Grant* was higher under any version of the Plan with *Imported reports*, especially all outcomes, suggesting the effect was more significant on the applicants' propensity to abandon than the examiners' propensity to grant. The increase could be due to Brazil importing reports from the IP5, which have higher grant rates (Sampat and Shadlen 2017; Mercadante and Paranhos 2022; IP5 2024b). Subsection 2.4.3 shows they indeed granted the twins more often than Brazil.

Table 2.3. Regression results for the likelihood of *Grant*

Variables	Entire analysis period				Plan period			
	All outcomes		Examiner decisions		All outcomes		Examiner decisions	
	I	II	III	IV	V	VI	VII	VIII
Imported reports		0.174***		0.046**		0.165***		0.050***
		(0.011)		(0.015)		(0.012)		(0.015)
Higher targets		0.037		-0.114***		0.051**		-0.117***
		(0.019)		(0.025)		(0.019)		(0.025)
Imported reports & Higher targets		0.056***		0.078***		0.048***		0.080***
		(0.008)		(0.011)		(0.008)		(0.011)
Family size	0.003***	0.003***	0.003***	0.002***	0.004***	0.004***	0.002***	0.002***
	(0.000)	(0.001)	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)
Constant	-0.069	-0.065	0.407**	0.413**	0.744***	0.784***	0.793***	0.828***
	(0.038)	(0.004)	(0.138)	(0.138)	(0.013)	(0.013)	(0.030)	(0.030)
Filing year	Yes***	Yes***	Yes***	Yes***	Yes***	Yes***	Yes***	Yes***
Outcome year	Yes***	Yes***	Yes***	Yes***	Yes***	Yes***	Yes***	Yes***
Observations	53,597	53,597	17,750	17,750	21,574	21,574	10,915	10,915
R^2	0.250	0.256	0.212	0.216	0.156	0.165	0.046	0.056

Robust standard errors are presented in parentheses. *5%, **1%, ***0.1%.

Higher targets affected examiners more than applicants, with mixed effects: no effect for all outcomes in the entire analysis period, a positive effect for all outcomes in the Plan period, and negative effects for examiner decisions in the entire analysis period and in the Plan period. Applications prosecuted under both treatments also had the highest positive effects for examiner decisions, which is counterintuitive given the effects associated with each treatment alone. These conflicting results suggest a selection bias.

As explained in Section 2.2, applications under *Higher targets* alone (OA 6.22) qualified for the Plan and, despite being filed before 2017, had no report to be imported from other offices. This could be because these inventions are more complex, and even the examiners from other offices were having a harder time defining the relevant prior art. Subsection 2.4.3 shows that applications under *Higher targets* alone belonged to families less frequently filed and granted elsewhere. Since these offices were not under *Higher targets*, other factors were affecting the grant rate. Another explanation relate to these application being filed by Brazilian applicants, who are less likely to file abroad, explaining the absence of a report to import. Brazilians filed 96.5% of applications with only *High targets* but less than 10% of all other subsamples.[29] Future studies should analyse what is behind this selection bias.

Comparing applications under both treatments with those under *Imported reports* alone, *Higher targets* increased the likelihood of *Grant* for examiner decisions. A similar bias would not be present, or at least not as relevant, in these cases because there were reports to import

[29] Brazilians filed 4.1% of applications outside the Plan before the Plan period, 8.1% outside the Plan during the Plan period, 1.2% under *Imported Reports* alone, and 2.1% under both treatments.

and because the share of Brazilian applicants was much smaller. Therefore, *Higher targets* led examiners to grant more often, so the applications prosecuted under OA 6.22 had a lower grant rate because of other characteristics than the Plan itself.

This analysis also investigated the Plan's influence on the likelihood of grants without examiner objections, or a *Direct grant*, as shown in Table 2.4. The results for the entire analysis period are almost identical to those in the Plan period. *Higher Targets* alone had small effects in all scenarios, especially for examiner decisions. There were much bigger positive effects associated with examiner decisions under *Imported Reports* alone and under the two treatments together. Again, the combination of the treatments had the biggest effects. Thus, on top of making examiners grant more often, the Plan increased the chances of them granting without any objection, and the most important mechanism behind these effects is importing another office's prior art search reports. As explained in Subsection 2.3.3, this effect on *Direct grant* means more patents were granted exactly as filed, with broader scope of protection.

Table 2.4. Regression results for the likelihood of *Direct grant*

Variables	Entire analysis period				Plan period			
	All outcomes		Examiner decisions		All outcomes		Examiner decisions	
	IX	X	XI	XII	XIII	XIV	XV	XVI
Imported reports		0.109***		0.121***		0.107***		0.121***
		(0.008)		(0.013)		(0.009)		(0.013)
Higher targets		0.026		0.003		0.024		0.003
		(0.012)		(0.019)		(0.013)		(0.019)
Imported reports & Higher targets		0.090***		0.183***		0.087***		0.183***
		(0.006)		(0.011)		(0.006)		(0.011)
Family size	0.001***	0.000	0.001***	-0.000*	0.001***	0.001**	0.001***	-0.000
	(0.000)	(0.000)	(0.000)	0.000	(0.000)	(0.000)	(0.000)	(0.000)
Constant	-0.017	-0.013***	0.142	0.147	0.896***	0.941***	0.857***	0.929***
	(0.002)	(0.002)	(0.101)	(0.100)	(0.006)	(0.006)	(0.013)	(0.013)
Filing year	Yes***	Yes***	Yes***	Yes***	Yes***	Yes***	Yes***	Yes***
Outcome year	Yes***	Yes***	Yes***	Yes***	Yes***	Yes***	Yes***	Yes***
Observations	53,597	53,597	17,750	17,750	21,574	21,574	10,915	10,915
R^2	0.090	0.107	0.125	0.154	0.045	0.063	0.069	0.102

Robust standard errors are presented in parentheses. *5%, **1%, ***0.1%.

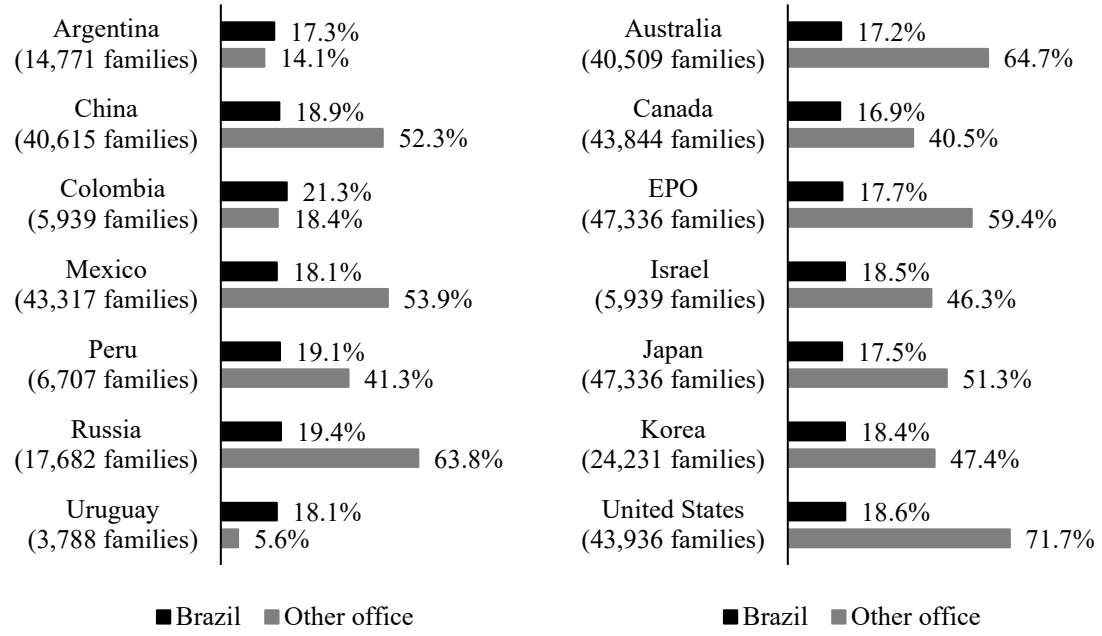
Turning to the control variables, invention importance and year fixed-effects were significant in all regressions. An extra twin in the family made a *Grant* more likely in all regressions, affecting applicants more than examiners, but had almost no effect on *Direct grant*.

The descriptive statistics in Subsection 2.3.5 showed the increase in grant rates, and the regressions show that the Plan led to grants being more likely and to an even larger increase in the likelihood of granting without examiner objections. The Plan's most significant effect was making examiners adopt another office's search report. Forcing examiners to decide faster also contributed to the increase despite the selection bias for applications prosecuted under OA 6.22.

2.4.3 Are Brazilian grant rates unique?

This study also compared grant rates from the INPI and 14 other offices to understand if Brazil has been following an international trend or going down an independent path. Using the sample of 48,913 families defined in Subsection 2.3.4, the grant rates were estimated for Brazil and each other office considering the family cohorts that have at least one twin from both. As shown in Figure 2.7, Brazil only has a higher grant rate than Argentina, Colombia, and Uruguay. Thus, the INPI stands out by granting less often than all offices from the Global North and most from the South.

Figure 2.7. Grant rates for shared families

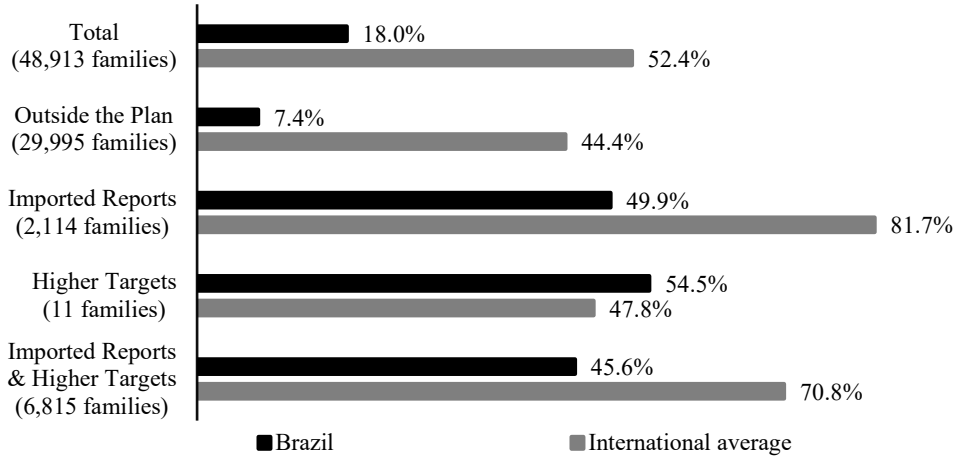


Note: Brazil was paired with each other office one at a time, and the grant rates were estimated considering the cohort of families with at least one twin in both offices. The number of families in each cohort is indicated in parentheses below every other office.

In Figure 2.1, the families were separated across four subsamples. There is only one control subsample because more than half the families had at least one twin decided before and another during the Plan period but outside the Plan. The first result was that those outside the Plan had the lowest rates for Brazil and the international average. This subsample includes much older decisions than the treated subsamples. If the rest of the world has also increased the average grant rate over time, as Brazil had, the treated subsamples might have higher grant rates because of a selection bias for more recent outcomes. This cannot be confirmed since the data did not include the outcome date for the other offices, but the IP5 reported almost uninterrupted growth in grant rates over the last decade (IP5 2024b). Still, if grant rates have increased internationally over time, the Brazilian rates increased more rapidly.

The average international grant rate for families under *Imported Reports* was 37.3pp higher than outside the Plan. In Brazil, the rate was 42.5pp higher. Assuming the international gaps capture systemic differences among these families, *Higher targets* led to a 5.2pp marginal increase in Brazilian grant rates. Repeating the analysis for families under *Imported reports* and *Higher targets*, the average international rate was 26.4pp higher than the control, while the Brazilian rate was 38.2pp higher. Thus, both treatments combined led to an 11.8pp marginal increase in grant rates. Meaningful conclusions cannot be drawn from the subsample under *Higher Targets* since only 11 families had a twin in another office. However, that also indicates a possible selection bias (see Subsection 2.4.2).

Figure 2.8. Summary of international comparisons of grant rates (%)



In summary, Brazil historically had lower grant rates than most countries, even in the Global South. However, the Plan has been increasing the grant rates beyond the international trend for twins in the same family. In Section 2.6, these results are combined with the findings about *Grant* and *Direct grant* rates to argue that the Plan might be reducing the examination rigour in Brazil, discuss what that could mean for patent quality, and propose how this decline could be tested in further studies.

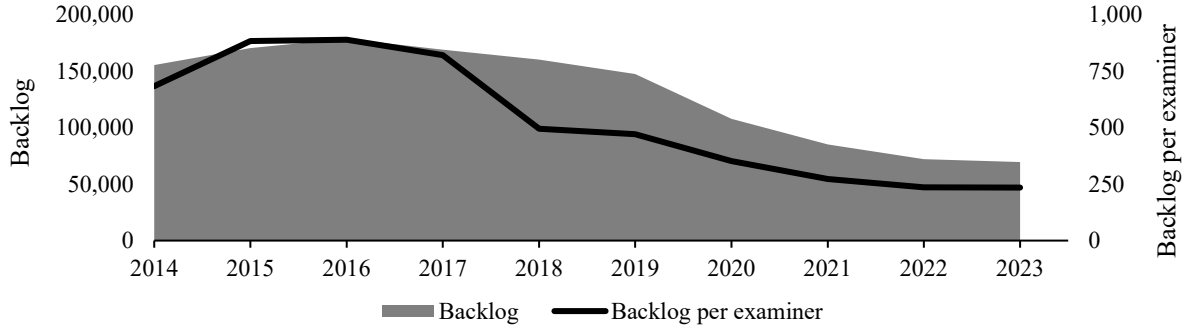
2.5 The INPI and the Brazilian backlog in international comparison

Although every patent office struggles with pending applications, the issue has been acute in Brazil (Shadlen 2017; Mercadante and Paranhos 2022). Drahos (2010, p. 251) reported that the USTR 'cited the backlog as one reason it was keeping Brazil on its Priority Watchlist in 2005', used to promote policy changes globally by threatening to impose trade sanctions (Shadlen 2017). Garcez Júnior and Moreira (2017) argued the Brazilian backlog contradicted

the right to a reasonable speed in public services, while Mercadante and Paranhos (2022) found it delayed prosecution and, especially for pharmaceuticals, triggered the term extension clause under which patents were valid for at least 10 years, something that the Supreme Court declared unconstitutional in 2021. This section analyses some production statistics from the INPI and compares them with offices from the IP5. Due to limitations in the data shared by these offices, comparisons are based on data on all applications, not just pharmaceuticals.

Figure 2.9 shows annual data on the backlog of applications pending final decisions, excluding applications for which substantive examination has not yet been requested, and the ratio per examiner. After peaking in 2016, the backlog has continuously fallen since the INPI hired new examiners in 2017. The biggest reduction was in 2020, led by abandonments after the publication of the Plan OA. There were 3,142 abandonments because applicants did not respond to the OAs that placed the prosecution under the Plan: one in 2018, 448 in 2019, 1,278 in 2020, 1,056 in 2021, and 359 in 2022. However, the reduction of the backlog has been slowing down, leading to 115,414 pending applications in February 2024 (INPI 2024b).[30]

Figure 2.9. Evolution of the backlog and the ratio per examiner



Note: Data obtained through the Access to Information Law.

Even though the INPI's efforts have reduced the backlog to a third of the ratio in 2015, this is still high. The backlog per examiner based on all applications, not just those with examination requested –, was 127 for the EPO, 425 for Japan, and 475 for Korea in 2022 (IP5 2024b). By the end of 2022, this ratio was 365 for Brazil.[31] Therefore, the Brazilian examiners have considerable workloads. Still, they have a high productivity. On average, each INPI examiner issued 94 decisions in 2022, while the examiners from the EPO issued 29, those from Japan issued 149, and those from Korea issued 176. In that year, the average lags from the first

[30] One might think the INPI has almost eliminated the backlog based on the Plan's official data (INPI 2024a), but this only covers the applications declared a target for the Plan in 2019. Many pending applications were excluded from the Plan initially and several have joined the backlog since, so the real size of the backlog is much larger.
[31] The ratio considering only applications with examination requested was 235.

action to the final decision in months were 20.4 for Brazil, 30.3 for the EPO, 4.8 for Japan, and 4.1 for Korea. In fact, the Brazilian examiners were already efficient in 2017, before the Plan was introduced: 51 decisions after nine months, on average.

In summary, the INPI has been under considerable pressure due to the ratio of pending applications per examiner. It has implemented policies to accelerate the prosecution and reduce the backlog, but the rate of reduction seems to be slowing down. The INPI examiners were already highly efficient compared to examiners from the biggest offices in the world. In that sense, a strategy like the Plan seems flawed in its design because the root of the delay in prosecution seems to be in the workload imbalance between the backlog and the number of examiners, not in examination efficiency.

2.6 Discussion

It is important to distinguish the Plan from all previous strategies for Brazilian examiners to incorporate someone else's input into the examination. The LPI established the PGO mechanism where any third party can submit documents to assist the examination. In addition, when patents are filed via the Patent Cooperation Treaty (PCT), which Brazil joined in 1978, the application comes with a search report and a preliminary non-binding opinion on its twin done by another office acting as an International Search Authority (WIPO 2024d). Brazil has also signed several Patent Prosecution Highway (PPH) agreements, which allow examiners to fast-track the prosecution of applications with a twin granted by a partner office, accessing all examination reports from the other examiner (INPI 2024d). Since substantive examination almost always happens in Brazil after other offices, examiners interviewed for this thesis said they have learned where to look for useful reports already published, including offices from developed and developing countries. Unlike the Plan, prosecution under any of these mechanisms means the INPI examiners may consult someone else's work but must do their own analyses based on the INPI's own guidelines and all patentability criteria in the LPI and are not forced to issue quicker decisions. On these important dimensions, the Plan is significantly different from other ways in which the INPI already uses someone else's work.

The Plan had an original target group of applications, which is close to being done with (INPI 2024a). However, one should expect the INPI to prosecute applications under OA 6.23 if they are not excluded from the Plan and there is a report to import. Since the INPI returned

the productivity targets under OA 6.23 to normal levels in 2023 (INPI 2023a), the new standard for the INPI has been to examine applications based on imported reports whenever possible.

As explained in Section 2.1, Japan and Korea have been outsourcing search reports since the 1990s (Drahos 2010; Yamauchi and Nagaoka 2015; Kim and Oh 2017). The Plan is not the same as these outsourcing strategies, but they are the closest possible comparisons because they make the examiner use someone else's prior art search. If these are examples of how outsourcing can strengthen patent examination, this should not be expected from the Brazilian policy for several reasons. Japan and Korea only outsource a limited number of applications per year. Their examiners tend to reserve outsourcing for less complex inventions. The outsourced report is done by accredited contractors who are trained and have their performance assessed by examiners from the patent offices. The report is done based on the offices' own guidelines, promoting homogeneity across decisions. Outsourcing is done to give examiners more time to focus on complex examinations instead of demanding faster decisions. Unsurprisingly, the Plan has produced different effects in Brazil than the Asian experiences. Apart from making examinations take longer, it has increased the likelihood of grant, even when compared to other offices to control for characteristics of the patent families, and of grant without examiner objections.

Since the Asian policies have also led to fewer appeals, which are also less frequently successful, it is helpful to analyse the INPI's report on second-stage examination: appeals to rejections and third-party post-grant oppositions (INPI 2023b).[32] The INPI's decisions have become more contested, even considering the slight fall in the rate of opposition – which resulted from opposition not keeping up with the impressive growth in the number of grants.[33] Meanwhile, the success rate for appeals against rejections is growing and has been above 50% since 2016, while the success rate for post-grant oppositions has fluctuated around 45%. Thus, contrary to the results in Japan and Korea, the pro-grant bias of the INPI in recent years is also observed in appeals and opposition, which might be driving agents to file more appeals against rejections and fewer post-grant oppositions, making litigation a better option. There is also a significant backlog of pending appeals (6,684) and oppositions (210), with only a few

[32] The data included applications from all technical fields.

[33] In absolute numbers and considering all technical fields, rejections fell 12.4% from 2018 to 2022, but appeals grew 32.8%, meaning the rate of appeals against rejections has grown continuously from 28.5% to 43.3%. On the contrary, grants grew 152.1%, and oppositions grew 47.8% in absolute numbers, which meant the rate of opposition fell from 0.9% to 0.5%.

examiners qualified for second-stage examination. The combination of these results reinforces the view that developing countries cannot rely on post-grant correction measures (Correa 2000; Drahos 2008; 2010; Shadlen 2013; 2017; Sampat and Shadlen 2015).

It is important to compare these experiences since the then General Patent Coordinator at the INPI wrote a report in 2018 as part of a training programme at the Japanese office, suggesting lessons on outsourcing. Latsch (2018, p. 38) concluded that outsourcing was not the best option for Brazil, suggesting the importation of search reports as a better option while stressing that 'the main recommendation is ensuring adequate work capacity, maintaining the effort to hire new patent examiner, improving the work-sharing by the pre-examination program and by improving the Information Technology tools for exchange patent information'.

Another question related to where Brazil is importing the reports from. The Plan consists of looking for reports from the IP5, but examiners from the INPI said in interviews for this thesis that, in most cases, they only use reports from the United States or the EPO. These offices have much higher grant rates than the INPI, comparing applications from the same patent families, as shown in Subsection 2.4.3. Therefore, it is not surprising that this policy has increased the Brazil grant rate. In addition, examiners from other offices might not search the INPI's database, especially due to language restrictions, which might create a bias against Brazilian inventors that only file domestically. Thus, the international report might ignore these applications when defining the relevant prior art. If the INPI examiners cannot conduct additional searches, this system might discriminate against Brazilian prior art.

One may oppose using someone else's prior art searches altogether because this is a key step for the examiners to prepare for the analysis of the invention (Drahos 2010), which was confirmed by examiners from the INPI in interviews for this thesis. Likewise, one may oppose it because examiners are less swayed by prior art cited by anyone else (Cotropia et al. 2013). When patent offices use someone else's reports instead of hiring new examiners, they may also increase the effects of examiner seniority: granting more often, citing less prior art, and restricting less what is granted (Lemley and Sampat 2012). Indeed, examiners granted more often and made objections before granting less often under the Plan.

The Plan also went beyond importing reports, forcing examiners to decide faster by increasing their productivity targets. The results of this study are in line with the suggestion from other authors that faster decisions lead to grants happening more often, with broader scope and lower quality (Frakes and Wasserman 2017; 2023; Kim and Oh 2017; Marco et al. 2019).

Although promoting efficiency in examination is important to guarantee the balanced stimuli of patents (Macdonald 2002; Granstrand 2005; Andersen 2006; Rockett 2010), there might be benefits in some delay to prosecution to reduce informational constraints (Nagaoka and Yamauchi 2022). Applicants may also have strategic interests in delaying prosecution (Harhoff and Wagner 2009), with studies showing evidence of this behaviour regarding pharmaceutical applications (Mercadante et al. 2018; Zhu et al. 2022).

In that sense, the empirical analysis of the Backlog Plan and the comparison with international experiences of outsourcing prior art searches and increasing productivity targets shows how the Plan is flawed by design and has more effectively increased the grant rate than accelerated the prosecution and reduced the backlog, as originally intended. Examiners are making fewer objections before granting patents under the Plan. Also, the grant rates under the Plan have grown more rapidly than in other offices, comparing the same patent families, which means there is a marginal effect being intrinsic characteristics of the families. The Plan is based on the incorrect assumption that slow examination was delaying prosecution in Brazil, when it was really caused by the backlog being too high for the number of examiners. The Plan might even have been unnecessary since it is unreasonable to assume examiners were not already checking the prosecution of twins by other offices. Lastly, importing reports from offices that grant more often should naturally bias the INPI towards more grants and may lead to discrimination against Brazilian prior art.

These results indicate that the Plan might be reducing the rigour of pharmaceutical patent examination in Brazil, which could lead to the harmful consequences of overprotecting innovation by granting low-quality patents. While this chapter cannot establish this causality, future studies should test this indication at the application level, investigating the scope of claims, examiner citations, opposition rates, or post-grant invalidation rates. Also, international comparisons should include countries like Egypt and India and detailed prosecution data like outcome dates and a distinction between pending, rejected and abandoned applications.

2.7 Conclusion

Without proper public debate, Brazil implemented the Backlog Reduction Plan, importing prior art searches from offices with high grant rates and forcing examiners to decide faster. This chapter has shown that this has set Brazil on a trajectory to grant more often and

request fewer changes to applications before issuing grants. Comparing grant rates internationally, this change is more significant than in other offices, indicating a marginal effect beyond intrinsic characteristics of the patent families.

The results show that the Plan has reduced the backlog, but the rate of reduction is now lower than before it was introduced when ignoring the initial wave of abandonments due to applicants failing to reply after being included in the Plan. This reduction in the backlog has allowed for an earlier start to the examination, making the overall prosecution faster despite the Plan prolonging the examination period.

The efficiency of Brazilian examiners was already comparable to that of some of the biggest patent offices in the world in terms of decisions per year and average examination lags. Therefore, the Plan was flawed in its design. If the biggest cause of the delay in prosecution was the backlog and if the INPI examiners were already that efficient, a productivity strategy based on cutting a part of the examination and forcing examiners to issue decisions quicker should not be as effective; the root of the delay remains, and the examiners are under more pressure.

Based on these findings and the empirical literature on similar policies, the Plan has been more effective in increasing the rate of grants and reducing how often examiners make objections before granting than its original goal: accelerating the prosecution and reducing the backlog, especially since it made examination take longer. Therefore, the Plan might be reducing the rigour of pharmaceutical patent examination in Brazil, which could lead to the granting of low-quality patents.

These trends should be discussed in the public forum to promote the strategy of using rigorous examination as a preventative measure against the negative consequences of overprotecting innovation in Brazil. In that sense, the INPI should effectively end the Backlog Plan and invest in hiring more examiners and strengthening internal examination capacities. For example, it may introduce more powerful search engines to assist examiners, but being mindful of the possible biases these tools could introduce and the possible effects on examination rigour. Also, Anvisa's non-binding PGOs are reports written for the same applications the INPI is examining and consider the same legislation. They should be more useful to inform, not substitute, the INPI examiner's decisions than another office's reports. It is a good sign that the INPI has hired 40 new examiners recently (INPI 2024e).

3 INFLUENCE AND CONVERGENCE TO HIGHER STANDARDS: THE DUAL EXAMINATION OF PHARMACEUTICAL PATENTS IN BRAZIL

Between 2001 and 2021, pharmaceutical patent applications filed in Brazil were examined by the patent office, the INPI, and the health regulator, Anvisa. This dual examination process meant that the INPI could only grant pharmaceutical applications related to products for human health if Anvisa also consented to the grant to promote examination quality and access to medicines (Shadlen 2011; 2017; Guimarães and Corrêa 2012; Guimarães 2019). Notwithstanding the possible effects on prosecution outcomes, this chapter draws lessons for the debate on patent policies to address public health challenges by analysing the influence of this dual examination system on what is considered relevant grounds for negative decisions on pharmaceutical patent applications, i.e. a rejection from the INPI or a denial of consent from Anvisa. Since both entities examined applications based on the same patentability criteria, this study compares negative decisions to see if there are systemic differences in how the entities examine the applications and if the dual examination system led to one entity influencing another.

Anvisa's prior consent stands out as the most intense experience any country has had with patent offices and health regulators cooperating in patent examination. Yet, this type of cooperation has a precedent in Brazil. The 1882 Decree nº 8,820 determined that prior consent was necessary for pharmaceutical, chemical, or agricultural products, for inventions that were not industrially applicable, and for inventions considered contrary to morals, good manners, safety, *ordre public*, or public health. Pharmaceutical applications would be examined for potential risks to public health by the Central Board of Public Hygiene.

Similar policies have been introduced or at least proposed in other countries.[34] Proposals for the Ministry of Health to be involved in patent examination were discussed in the Argentinian Congress in the 1990s, but no such policy was introduced (Shadlen 2017). In 2002, Egypt established in the Law No. 82 that, before granting applications with health significance, the patent office must send them to the Ministry of Health, which may submit oppositions. Similarly, Paraguay determined in the 2005 amendment to the Law No. 1630/2000 that patents related to pharmaceutical products required a technical opinion from the Ministry of Health before being granted. The Presidential Degree No. 29004/2007 in Bolivia also tried to introduce prior consent from the Drugs and Health Technology Unit for pharmaceutical

[34] Although included in patent laws, no evidence of these measures being implemented was found.

applications, but Congress never ratified this proposal. Even the United States has been investigating how to combine knowledge and assets from both entities to make sure pharmaceutical companies cannot 'unjustifiably delay generic competition based on trivial changes to a drug product' (USPTO 2022 para. 5).

These proposals explore the policy flexibilities within the TRIPS Agreement. One key principle of TRIPS is that 'members may, in formulating or amending their laws and regulations, adopt measures necessary to protect public health' (WTO 1994, Art. 8). In 2001, the Doha Declaration reaffirmed that TRIPS 'can and should be interpreted and implemented in a manner supportive of WTO members' right to protect public health and, in particular, to promote access to medicines for all [by using], to the full, the provisions in the TRIPS Agreement, which provide flexibility for this purpose' (WTO 2001, Art. 4).

Even though there is no clear definition of TRIPS flexibilities, they generally refer to which, when, or how inventions may be patented and how patent rights are exercised (Correa 2022). Many studies have investigated flexibilities related to pharmaceutical inventions like compulsory licencing, the Bolar exception, rights exhaustion, injunctions, Argentina's 2012 examination guidelines change, and India's Section 3(d) (Musungu and Oh 2006; Deere 2009; Correa 2014; 2022; Sampat and Shadlen 2015; 2017; 2018; t' Hoen et al. 2018; Sarnoff 2020; Oswald and Burri 2021; Tenni et al. 2022). Involving health authorities in the examination of pharmaceutical inventions is normally compared to the last two as measures to strengthen examination (Oswald and Burri 2021), especially to prevent patenting secondary pharmaceutical inventions (Correa 2014; Sampat and Shadlen 2015; 2017; 2018).

The use of flexibilities is also proposed as a response to TRIPS-plus policies that have been pushed especially by developed countries (Correa 2000; 2014; 2022; Deere 2009; t' Hoen et al. 2018; Shadlen 2017; Shadlen et al. 2020; Tenni et al. 2022). One example is the patent linkage mechanism, which prevents generic manufacturers from obtaining market authorisation while the drug is still protected by patents (Son et al. 2018; Raju 2022). Similarly, some clauses extend the patent term to compensate for the period when the invention was protected, but the drug has not yet been approved (Beall et al. 2019; Yang 2020). The rationale for these policies is that increasing private returns of patents promotes future innovative efforts.

If there are calls for cooperation to strengthen protection, assuming this promotes innovation, there should be no inherent issue with cooperation to strengthen examination. After all, a more rigorous examination based on the same patentability criteria should promote

balance in the patent system. The TRIPS-plus patent linkage mechanism also forces the health authority to extend the exclusivity of new drugs based on the patent office's assessment of the invention. Thus, two entities perform different tasks, but one is forced to incorporate the other's unrelated decisions. On the contrary, the dual examination system involves both entities performing the same task, and this chapter shows that the cooperation could be limited to the health authority's non-binding opinions on strategic applications.

The prominence of Anvisa's consent as a TRIPS flexibility has led to a vast literature on the topic, albeit limited in empirical data. Most focus on the history of bureaucratic and political conflicts and the changing guidelines (Shadlen 2011; 2017; Guimarães and Corrêa 2012; Abreu 2017; Guimarães 2019; Anvisa 2022a); others on the legal debate (Barbosa 2006; Basso 2006; Barbosa 2018; Di Blasi 2019). Yet, the empirical literature is restricted to small samples with data mostly from the early 2000s (Silva 2008; Sampat and Shadlen 2015; 2017) or broad analyses of the influence on the outcome (Mercadante and Paranhos 2022).

This chapter aims to produce a more conclusive understanding of how health authorities can contribute to pharmaceutical patent examination by investigating the grounds for negative decisions on pharmaceutical patent applications cited by examiners from the INPI and Anvisa. This analysis is possible because the two entities applied the same patentability criteria, based on the articles of the LPI, only varying in how frequently they cited each article. Since the focus is on which issues were more frequently considered serious enough to warrant a negative decision, the analysis is restricted to negative decisions issued by the entities and does not evaluate the prosecution outcomes. The sample includes decisions over two decades to analyse changes in each entity's examination standards. Since one entity only examined the application after the other had reached a decision, this chapter also investigates if some of the changes in standards might indicate that the entities were influencing each other's standards.

The findings show that, at first, there were significant differences in the grounds cited since the INPI focused on traditional patentability criteria while Anvisa had a more diverse approach. Over time, the entities converged to higher and more diverse citation patterns. The biggest change happened in the INPI, whose decisions became closer to Anvisa's than its own from earlier years, suggesting the entities influenced each other, especially by giving higher relevance to invention description, which is important to promote balanced stimuli in patenting. There is also evidence of Anvisa affecting the outcome and that the INPI benefited from Anvisa's decisions even while rejecting any cooperation. Thus, based on this experience, the

dual examination mechanism can increase the rigour of pharmaceutical patent examination and, depending on how this policy is designed, produce an almost symbiotic and mutually beneficial relationship. This might be a useful strategy to counterbalance the hardening of patent systems, especially for other countries in the Global South, but also those in the North.

The remainder of this chapter has five sections. First, a summary of the key rules of the Brazilian system of pharmaceutical patent examination and the prior consent mechanism. Next, a definition of the research aims, the empirical strategy and the data collection and management processes and a presentation of some statistics about the frequency of negative decisions. The Results section analyses how frequently each entity cited the different grounds for negative decisions over the two decades. Then, the findings are discussed based on the empirical literature on prior consent and the more general literature on TRIPS flexibilities. Finally, the Conclusion has lessons for any country interested in similar policies.

3.1 The Brazilian pharmaceutical patent system

After becoming party to the TRIPS Agreement in 1994, the most significant reform Brazil had to implement was reintroducing pharmaceutical patenting. Enjoying the flexibility under the previous treaties, such as the 1883 Paris Convention, it had excluded pharmaceutical products from patenting since 1945 and processes since 1969. In 1998, other 48 countries from the Global North and South applied similar restrictions to pharmaceutical products (WIPO 1988) to promote access to drugs and develop national industries (Chang 2001; May and Sell 2006; Orsi and Coriat 2006; Deere 2009). Although the deadline for the reform was 2005, Brazil did it in 1996 with the LPI (nº 9,279). Based on the timing of the reform and the mechanisms introduced, Brazil exceeded TRIPS's minimum requirements, considerably hardening patent protection (Shadlen 2017; Mercadante and Paranhos 2022; Reis 2022).

Before explaining the LPI, it is important to define how applications are examined. This chapter is focused on the substantive examination, where the examiner evaluates if the invention justifies giving the applicant a temporary exclusivity period for exploiting it commercially, so it ignores formal (e.g., having legal representation) or administrative (e.g., paying fees) requirements in the patent prosecution process.

This chapter analyses all articles of the LPI considered by examiners from the INPI and Anvisa as grounds for negative decisions, split into the four groups in Table 3.1. The first refers

to the traditional patentability criteria: novelty, inventiveness, and industrial applicability. Other criteria also mandated by TRIPS are the invention description group, the mailbox system for pharmaceutical products,[35] and the prosecution rules group. Some articles in the exclusions group are flexibilities explicitly allowed by TRIPS: banned substances, living beings, and health-related methods. It might seem odd that Anvisa's prior consent is not listed but although Anvisa examined the applications substantively, this mechanism was incorporated by the INPI as a formal aspect of the prosecution. If given, the patent could be granted, but consent denial was never considered grounds for rejection. Instead, it stopped the prosecution altogether.

Table 3.1. Key articles of the LPI regarding pharmaceutical patent examination

TRADITIONAL PATENTABILITY	
Novelty (Art. 11)	Inventions must not have been described in the state of the art.
Inventiveness (Art. 13)	Inventions must not be obvious to a person skilled in the art.
Industrial applicability (Art. 15)	Inventions must be suitable for industrial manufacturing.
INVENTION DESCRIPTION	
Description sufficiency (Art. 24)	Inventions must be sufficiently described so that a person skilled in the art can reproduce them.
Support for claims (Art. 25)	Claims must be supported by the description of the invention.
EXCLUSIONS	
Miscellaneous (Art. 10, I; II; III; VI)	Brazil does not consider inventions: discoveries; scientific theories; purely abstract conceptions; information presentation; and business schemes, plans, principles, or methods in mathematics, business, accounting, finance, education, publicity, prize draws, or surveillance.
Health-related methods (Art. 10, VIII)	Surgical, therapeutic, or diagnostic methods or techniques for human or animal health are not considered inventions.
Living beings (Art. 10, IX; Art. 18, III)	Living beings and biological materials found in nature are not considered inventions and may not be patentable, even if isolated, unless they are transgenic microorganisms that fit the patentability criteria and were not merely discovered.
Banned substances (Art. 18, I)	Inventions that are considered contrary to morals, good manners, safety, *ordre public*, or public health may not be patented.
Processes under mailbox (Art. 229-A)	Pharmaceutical or chemical process patent applications filed before the LPI entered into effect should be rejected.
PROSECUTION RULES	
Double protection (Art. 6; Art. 7)	The same invention may not be claimed in more than one patent application, prevailing the oldest.
Unity of invention (Art. 22)	Applications must include only one invention or a group of inventions that are connected by one inventive concept.
Split applications (Art. 26)	Applicants may split their applications if the divisional applications clearly reference and do not exceed the original.
Amendments (Art. 32)	Applicants may amend applications before substantive examination is requested but cannot expand the original invention object.

Created in 1970, the INPI had not examined pharmaceutical applications until the introduction of the LPI. Given this lack of experience and since Brazil only used two years of

[35] Brazil had to accept pharmaceutical product applications from January 1995, but only began examining them when the LPI came into force in May 1997, from which it also started accepting pharmaceutical process patents.

the 10-year deadline for pharmaceutical patenting, there were concerns over the rigour of patent examination since the office would have to hire and train new personnel. At the same time, Brazil implemented other TRIPS-plus policies, like the pipeline mechanism[36] and an automatic extension of patent terms.[37] It is in this context that Anvisa's prior consent was introduced as an amendment to the LPI in 2001.[38]

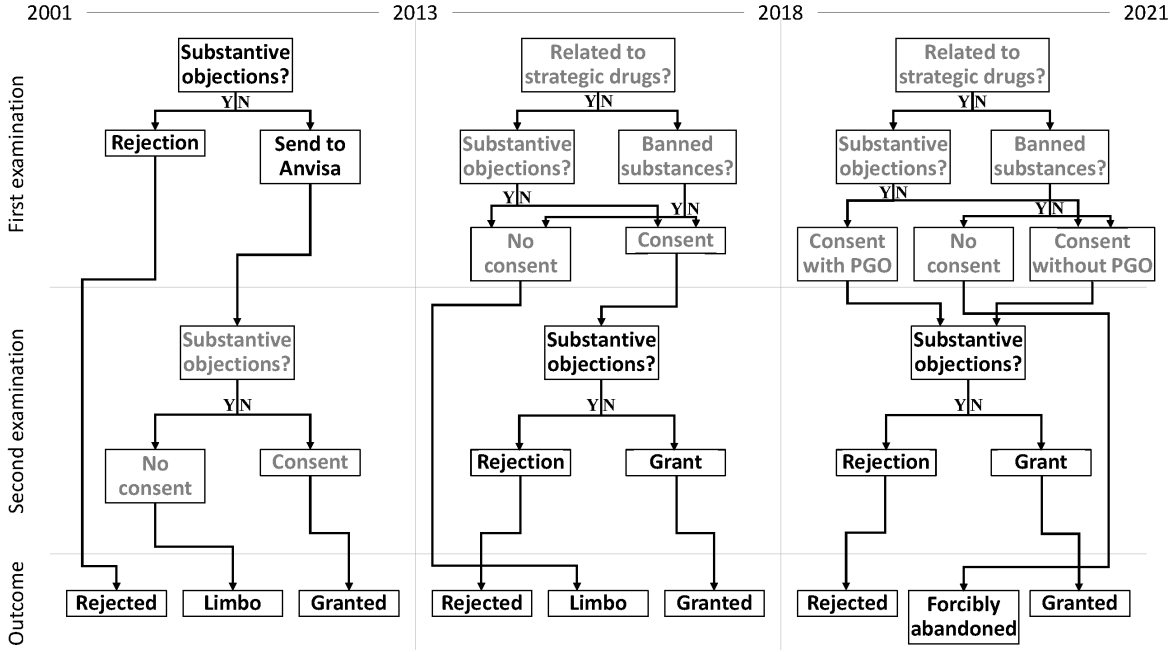
While the origins of prior consent arrangements are unclear, there are two main views. Some say it covered the lack of qualified personnel at the INPI. Given Anvisa's expertise in examining pharmaceutical technologies from a sanitary perspective, this dual examination process would increase patent examination rigour (Silva 2008; Abreu 2017). Others argue it was designed as or morphed into a strategy to prevent patenting secondary inventions (Shadlen 2011; 2017; Guimarães and Corrêa 2012; Correa 2014; Sampat and Shadlen 2015; 2017).

Regardless of policymakers' intentions, implementing the dual examination system proved complex. Shadlen (2017, p. 217) explains that Anvisa's help was initially welcomed 'when the patent office was overwhelmed by the tidal wave of applications it received in the new and complex area of pharmaceuticals, [but] the patent office came to regard health agency's participation as an inappropriate intrusion'. The constant clashing led to prior consent being reshaped several times by the Intellectual Property Inter-Ministerial Group (Abreu 2017; Guimarães 2019; Anvisa 2022a). Figure 3.1 tries to untangle this complex network.

From 2001 to 2012,[39] the INPI examined first and only sent to Anvisa the applications it intended to grant. Both entities considered all articles of the LPI, indicated in Figure 3.1 as an investigation of substantive objections. Anvisa's rationale to justify its involvement was that it had the duty to prevent the grants that could pose a health risk. The catch is the definition of health risk. Anvisa defended that a patent infringing any LPI article constituted a risk by restricting access to an invention that did not deserve protection. On the contrary, the INPI claimed to be the only entity that could examine patent applications. This disagreement led to applications being denied consent and staying in limbo unless abandoned by their applicants.

[36] This transitional mechanism allowed for the revalidation of pharmaceutical patents granted elsewhere, without being examined by the INPI, if the inventions had not been marketed anywhere and if there was no significant effort to develop them in Brazil. This was an incentive to the launch of new drugs in Brazil by granting patents that would have been rejected since the inventions were too old (Shadlen 2017; Mercadante and Paranhos 2022).
[37] The LPI established that patents were valid for 20 years from filing and at least 10 years from grant. This created an automatic extension regardless of what caused the delay or how long the extension would be. This mechanism was declared unconstitutional by the Supreme Court in May 2021 (STF 2021).
[38] Introduced by the Presidential Decree nº 2,006/1999, which later amended the LPI with Law nº 10,196/2001.
[39] The formal definition of how prior consent was assessed only came in 2008, with Anvisa's Resolution nº 45.

Figure 3.1. Flow chart of the prior consent mechanism



Note: The INPI's decisions are in black, and Anvisa's in grey. Split arrows follow left for *Yes* and right for *No*.

This policy was reshaped in April 2013 with Anvisa's Resolution nº 21, reversing the examination order. As the first to do it, Anvisa agreed to focus on applications related to strategic products for SUS. For those, it would consider all articles of the LPI. For all others, it would simply screen the applications for references to banned substances. In all cases, consent denial was still binding.[40] Still, the INPI maintained that Anvisa could not issue binding decisions, leaving applications with denials in limbo. There is one key difference between the two limbos. In the first period, it refers to applications that the INPI intended to grant, so applicants might have stayed hopeful, counting on prior consent being abolished. In the second period, applications had no decision from the INPI, so applicants might have been less hopeful.

The most important change happened in April 2017, when the entities signed the Joint Ordinance nº 1, introducing the last arrangement of prior consent until it was abolished by Law nº 14,195 in August 2021. Anvisa remained the first to examine but conceded even more, agreeing to deny consent only if applications referenced banned substances. Anvisa reserved the analysis of the other articles of the LPI for applications related to strategic products for SUS, and negative decisions in such cases were submitted as non-binding PGOs. Although Anvisa's PGOs were non-binding, the Join Ordinance determined that the INPI should justify any disagreement, making Anvisa's PGOs effectively stronger than those submitted by third

[40] An explanation of how Anvisa selected these applications is included in Appendix A.

parties. However, examiners and specialists in the subject interviewed for this thesis argued that the INPI normally addresses any PGO submitted before reaching a decision. Thus, there were three types of decisions: no consent, consent with PGO, and consent without PGO.

As a result, the INPI finally agreed to end prosecution after Anvisa denied consent, considering it a forceful abandonment (*arquivamento técnico*), and to deal with the applications in limbo that had not been abandoned. If Anvisa's decision in the previous periods cited banned substances, the application would be declared forcibly abandoned. Otherwise, the INPI would consider the decision a non-binding PGO and continue the prosecution.

Apart from reducing the conflicts between the entities, the Joint Ordinance also led to this mechanism being litigated less often. Before 2017, applicants often sought court orders for Anvisa to give consent, claiming it had no authority to examine patentability. Once Anvisa's main contribution became non-binding PGOs, applicants would have to argue that Anvisa had no right to submit a non-binding opinion. Since the LPI determines that any interested party may submit a PGO, this argument is much harder to defend.

The changes to workflow and guidelines produced three periods of the prior consent mechanism: February 2001 to March 2013, April 2013 to March 2017, and April 2017 to August 2021. The rest of this chapter refers to them as the first, second and third periods. The next section explains why negative decisions are a useful source for this analysis of cooperation between patent offices and health authorities and how applications from different periods were selected to compare the entities.

3.2 Methodology

This chapter is a case study of decisions issued by the INPI and Anvisa regarding pharmaceutical patent applications filed in Brazil. It investigates what types of issues are considered when both entities examine applications by looking at the grounds for negative decisions. However, there were several changes to the dual examination mechanism over the two decades, as explained in Section 3.1. Applications were examined by one entity at a time, with the examination order reversed after the first period. The second and third periods also changed the process of determining which applications required Anvisa's prior consent, the articles of the LPI that Anvisa considered, and the binding power of its decisions.

Considering the complexity of these processes, this section is divided into two parts. First, it explains why negative decisions are especially useful for analysing patent examination standards. Then, it presents the data collection and management strategies, a general characterisation of how frequently both entities decided negatively, and the empirical strategy for analysing grounds for negative decisions.

3.2.1 The usefulness of negative decisions

Negative decisions like the INPI's refusal or Anvisa's denial of consent are interesting documents because examiners from both entities consider the same articles of the LPI and must clearly state which articles are being infringed, or else applications are presumed patentable. Thus, it informs exactly what patentability criteria the examiner considered relevant. By analysing the universe of negative decisions, one can infer which articles of the LPI are more frequently cited as grounds for rejection. Changes to the citation rate can have two explanations. If Article A is cited more than Article B, it might be that more applications have an A-type issue or that examiners pay more attention to these issues than those related to Article B. In both cases, the most frequently cited articles are more relevant grounds for rejection. One can also learn from negative decisions when the entities disagreed completely (one positive and one negative decision) or partially (two negative decisions citing different articles). In that sense, negative decisions show if some grounds are more relevant for one entity than the other. Furthermore, this thesis considers that the more articles are cited frequently, the greater the examination rigour is since a wider range of criteria is often considered relevant.

In contrast, one can only learn from positive decisions like the INPI's grant or Anvisa's consent that the specific version of each application was considered patentable. It is impossible to infer which articles were more relevant for the examination, and applicants may make amendments during the prosecution as demanded by the examiners or of their own volition. Therefore, to learn more from positive decisions, one must compare the final version of the application with the original filing and read all communications between examiners and applicants to determine what was changed, why, and by whose initiative. Doing so would require considerable analytic resources and access to many documents for each application, thus affecting the sample size.

Therefore, this chapter focuses on negative decisions to understand and compare the entities' decisions by identifying observable indications of what issues were more relevant.

While an analysis of all communication provides a complete understanding of the examination process, negative decisions alone should have enough meaningful information but still allow for a larger sample. Thus, the research goal is to estimate how frequently the entities cited each article of the LPI as grounds for negative decisions. With this, one can understand if having the health authority cooperate with the patent office in the examination of pharmaceutical applications led to other issues being considered relevant, based on the different workflows and guidelines of the prior consent mechanism.

3.2.2 Data and empirical strategy

The data was collected from primary and secondary sources, creating multiple samples. First, all decisions from 2001 to 2021 were identified, and each entity's frequency of negative decisions was estimated. Then, the negative decisions issued by each entity were selected to investigate the citation patterns of the different articles of the LPI. This subsection explains the methodological choices to identify them.

The data on INPI decisions was extracted from the Autumn 2022 edition of the EPO's PATSTAT database, covering applications filed in Brazil from 1995 to 2020 (EPO 2024a). Seven categories of applications were discarded: a) pipeline applications;[41] b) utility models; c) certificates of addition; d) applications without a decision from the examiner, i.e. abandoned, still pending; e) applications whose outcome could not be coded due to missing or unclear legal event data on PATSTAT; f) applications with an outcome after 2021, to restrict the analysis to the period when both entities were examining applications; and g) applications not classified as primarily pharmaceutical based on IPC codes.[42] Using these criteria, there were 15,821 applications granted or rejected by the INPI.

Next, data was extracted from Anvisa's prior consent records (Anvisa 2022b). Only the last decision was considered for applications examined by Anvisa more than once. The analysis

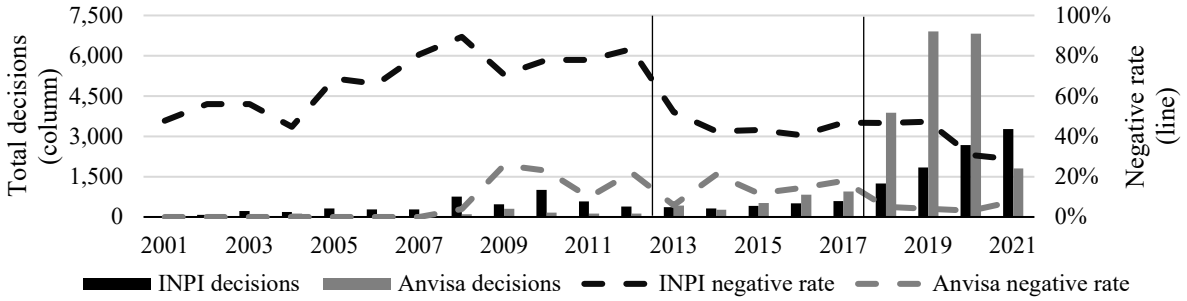
[41] Pipeline applications could not be included because the INPI only did a formal analysis, and Anvisa examined substantially 247 applications, giving consent to 224 (90.1%). Anvisa representatives explained that they examined if the applications would have been patentable if the LPI were in effect on the priority date.

[42] Applications can have multiple IPC codes, leading them to be considered as, for example, both pharmaceutical and chemical. Using the weighted concordance between IPC and NACE codes by Eurostat (2015) available in PATSTAT, this chapter considers pharmaceutical applications are those with the code IPC A61K (except A61K 8/*) or with that code associated to A61P, C07D, C07H, C07J, C07K, C12, C12P, or C12Q, as long as the weighting system for multiple codes indicates that the applications are at least 75% pharmaceutical.

also ignored pipeline applications, utility models, certificates of addition, and those without a decision before prior consent was abolished,[43] leading to 23,681 decisions from Anvisa.

Using these samples, each entity's rate of negative decisions was estimated, as shown in Figure 3.2: 48.4% for the INPI and 6.0% for Anvisa. However, not much can be learned by comparing these rates for two main reasons. Anvisa's rate is biased by the share of positive decisions limited to banned substances, a key information missing from the records, and this significantly affects the likelihood of a negative decision.[44] The evolution of the rates is also influenced by changes to the examination order guidelines. Therefore, one should not read too much into the differences in rates. Still, almost all (91.7%) negative decisions in the third period were consents with PGOs, and the INPI withheld applications until the 2017 Joint Ordinance.[45]

Figure 3.2. Total decisions and rate of negative decisions per entity and decision year



Note: The vertical lines roughly separate the three periods of prior consent.

Applications that received negative decisions were selected for the main analysis, and the respective decision documents from Anvisa and the INPI were extracted from the INPI's Buscaweb database in December 2023 (INPI 2024f). A quarter of the more than 4,000 applications searched for on Buscaweb were discarded due to missing documents. Then, decisions were read to identify which articles listed in Section 3.1 were cited. However, the entities were not examining the same applications at the same time. The entity acting as 'second to decide' could see the decision published by the other entity. There were also different workflows and guidelines throughout the two decades, impacting which applications were selected and how Anvisa examined them. Therefore, this study used two samples per entity: one as the first and another as the second to decide.

[43] There are five explanations: a) Anvisa considered inventions did not need prior consent; b) applications were abandoned before Anvisa reached a decision; c) prior consent was abolished while Anvisa was examining; d) the INPI cancelled the forwarding to Anvisa before any decision was made; or e) the INPI changed their mind and issued a rejection after Anvisa substantive requests before issuing its decision as the second entity to examine.
[44] Distinguishing between these decisions would require reading all of them only to discard many, if not most.
[45] Considering all applications reported by Anvisa, 2,087 were sent in the first period, 8,569 in the second, and 20,346 in the third. In 2018, Anvisa received almost as many applications as in all previous years combined.

The samples for the INPI were restricted by data availability and the changes to the dual examination mechanism. The INPI was the first to decide in the first period, and there is no way of knowing if the INPI would have sent these applications to Anvisa had it given them a positive decision. Thus, these applications were included based on the assumption that any grant would have required Anvisa's consent given the classification as mainly pharmaceutical.

The INPI was the second to decide in the second and third periods. However, it refused to continue prosecuting applications with a negative decision from Anvisa until the entities signed the 2017 Joint Ordinance. Thus, the INPI only issued second decisions in the second period when Anvisa's first decision was positive. Since Anvisa's records of positive decisions do not say when it considered all articles of the LPI or simply banned substances. This distinction is crucial because an equivalent decision from Anvisa, based on all articles, should be more influential on the INPI than one restricted to banned substances. To avoid this imprecision, this study focused on applications with a negative decision from Anvisa, investigating the INPI's negative decisions as the second to decide in the third period.

Thus, there were two types of negative decisions from the INPI: rejections as the first to examine in the first period and rejections in the third period after Anvisa gave consent with PGO. The latter included applications that had been left in limbo but, after the 2017 Joint Ordinance, the INPI considered had consent with PGO (see Section 3.1). Random cohorts proportional to the total of each decision year were selected and the available documents were extracted from Buscaweb, resulting in a sample of 1,438 negative decisions from the INPI: 1,180 as the first and 258 as the second to decide.

Lastly, negative decisions reported on Anvisa's records were searched for on Buscaweb, considering that Anvisa gave consent with PGO if consent was mandated by a court order and ignoring decisions based solely on banned substances to compare equivalent decisions from both entities. Many negative decisions were excluded, especially from earlier years, because of missing decision documents. Since Anvisa was the second to decide in the first period and the first to decide in the second and third periods, its sample had 1,151 negative decisions: 1,142 as the first and just nine as the second to decide.

3.3 Results

The grounds for 1,180 first negative decisions by the INPI and 1,142 by Anvisa were coded based on the four groups of articles: traditional patentability, invention description, exclusions,[46] and prosecution rules. Table 3.2 presents the number of decisions per entity as the first and second to decide and how often they cited each article of the LPI.

Table 3.2. Grounds for negative first and second decisions per entity

Grounds	First to decide				Second to decide			
	Anvisa (1,142 decisions)		INPI (1,180 decisions)		Anvisa (9 decisions)		INPI (258 decisions)	
	N	%	N	%	N	%	N	%
Traditional patentability	**817**	**71.5**	**1,009**	**85.5**	**3**	**33.3**	**229**	**88.8**
Novelty	558	48.9	385	32.6	0	0.0	123	47.7
Inventiveness	608	53.2	897	76.0	3	33.3	221	85.7
Industrial applicability	9	0.8	5	0.4	0	0.0	1	0.4
Invention description	**917**	**80.3**	**498**	**42.2**	**6**	**66.7**	**197**	**76.4**
Description sufficiency	827	72.4	300	25.4	4	44.4	111	43.0
Support for claims	909	79.6	458	38.8	6	66.7	194	75.2
Exclusions	**529**	**46.3**	**341**	**28.9**	**0**	**0.0**	**85**	**32.9**
Miscellaneous	5	0.4	0	0.0	0	0.0	0	0.0
Health-related methods	426	37.3	211	17.9	0	0.0	58	22.5
Living beings	124	10.9	75	6.4	0	0.0	21	8.1
Processes under mailbox	0	0.0	98	8.3	0	0.0	0	0.0
Prosecution rules	**254**	**22.2**	**20**	**1.7**	**1**	**11.1**	**52**	**20.2**
Double protection	47	4.1	3	0.3	0	0.0	12	4.7
Unity of invention	36	3.2	11	0.9	0	0.0	18	7.0
Split applications	5	0.4	0	0.0	0	0.0	0	0.0
Amendments	182	15.9	6	0.5	1	11.1	25	9.7

Note: This table indicates how many decisions from each entity as the first or second to decide cited each article. Since negative decisions typically cite multiple articles, the group totals are not the sum of each part. The group totals indicate how many decisions from each entity as the first or second to decide cited at least one article from that group. For example, 558 (or 48.9% of the 817) first decisions from Anvisa cited novelty, and 817 (or 71.5% of the 1,142) first decisions from Anvisa cited at least one traditional patentability article.

Traditional patentability was the most frequent group in the INPI's first decisions (85.5%) and a close second place for Anvisa (71.5%). Both rarely cited industrial applicability, which makes sense for pharmaceutical inventions. The other criteria had mixed results for the entities. While both cited inventiveness more often than novelty, the INPI cited it more often than Anvisa (76.0% and 53.2%) but cited novelty less often than Anvisa (32.6% and 48.9%). Some observers have suggested that Anvisa's prior consent specifically acted against the protection of secondary inventions (Shadlen 2011; 2017; Guimarães and Corrêa 2012; Correa 2014; Sampat and Shadlen 2015; 2017). Silva (2008) explained that applications claiming a

[46] The article about banned substances is not included here because Anvisa's decisions limited to this were ignored, as explained in Subsection 3.2.2. The INPI never cited that as grounds for the rejections included in this study.

second use received negative decisions from Anvisa based on novelty. Therefore, the results for this group might reveal a difference in the scrutiny of specific applications and framing of oppositions: the INPI was more focused on inventiveness, and Anvisa often also cited novelty.

The increase in the citation rate of traditional patentability comparing the INPI's first and second decisions (from 85.55 to 88.8%) was led by novelty being cited more frequently (from 32.6% to 47.7%), reaching roughly the same level as Anvisa's first decisions (48.9%). This suggests that Anvisa might have influenced the INPI.

Anvisa cited the invention description much more frequently in first decisions (80.3%) than the INPI (42.2%). Both cited the lack of support for claims more often than general issues with the description. One possible explanation might be the complex processes of the prior consent mechanism (see Appendix A). Anvisa had to identify which applications were related to strategic products for SUS to determine when to consider all articles of the LPI or simply screen the documents for references to banned substances. Thus, it might have paid more attention to how inventions were described.

The INPI's citation rate of invention description articles as the second to decide (76.4%) is almost the same as Anvisa's rate as the first to decide (80.3%) and much higher than its own rate from first decisions (42.2%). Thus, deciding after Anvisa, which seems to have paid more attention to these articles, probably led the INPI to consider them more frequently.

The group of exclusions was cited less often by Anvisa (46.3%) than the INPI in first decisions (28.9%). The most common article for both entities relates to health-related methods: 37.3% for Anvisa and 17.9% for the INPI. As the health regulator, it is logical that Anvisa would care more about this. Meanwhile, the INPI rejected many process applications filed through the TRIPS-mandated mailbox system, and Anvisa never cited this in the decisions analysed. However, this makes sense because the system was created exclusively for product applications filed before May 1997, and the INPI could easily identify this as the first to decide.

The change in the overall citation rate of exclusions in the INPI's first and second decisions seems small: from 28.9% to 32.9%. However, it is more impressive if one considers that the specific clause about processes under mailbox no longer applied. Ignoring that article, the overall rate increased from 22.7% to 32.9%. Again, Anvisa probably influenced this shift.

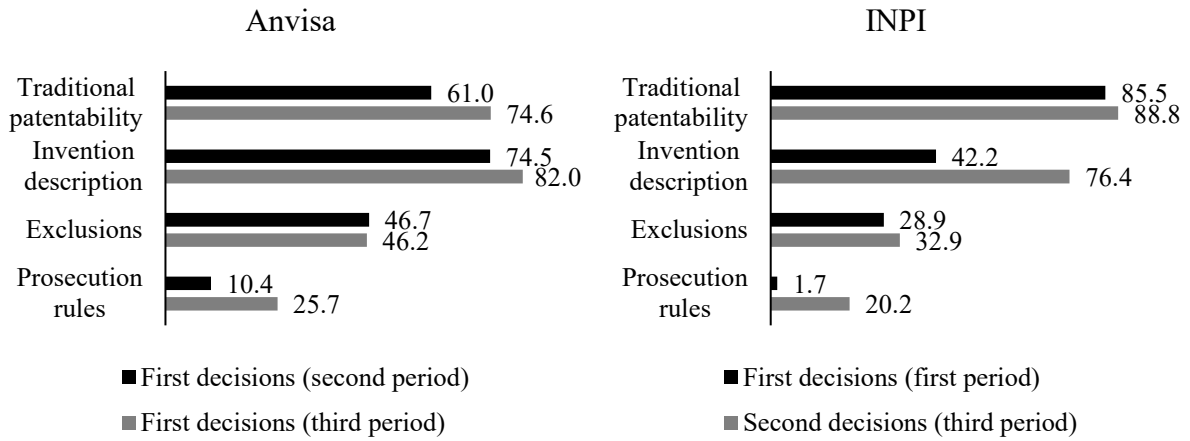
Even though it was the least frequent group for both entities, there was a significant difference in citation rates of prosecution rules as the first to decide: 1.7% for the INPI and

22.2% for Anvisa. It might be that the greater attention paid to invention description led to the issues with prosecution rules becoming more apparent. For example, a more careful analysis of how the invention is described might make it easier to see that an amendment introduced a claim that expanded the object of the invention.

Once more, the citation pattern of the INPI's decisions as second (20.2%) was similar to Anvisa's as first (22.2%), suggesting another influence. The most significant change in citation rates for the INPI was for amendments, which grew from 0.5% to 9.7%.

Figure 3.3 summarises the comparison of citation rates aggregated by groups of articles. For the INPI, 1,180 first in the first period were compared with 258 second decisions in the third. Since this study could only analyse nine decisions from Anvisa as the second to decide, it analysed the evolution of rates in first decisions in the second (259) and third periods (883).

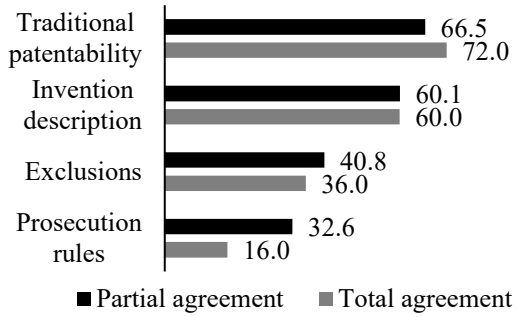
Figure 3.3. Evolution of citation rates in negative decisions of each group of articles per entity as the first and second to decide



Again, the INPI's second decisions in the third period were closer to Anvisa's first decisions in that same period than its own first decisions in the first period. This may be a sign that Anvisa had some influence over the INPI by bringing attention to other groups of articles of the LPI. Anvisa also increased its citation rates, especially regarding traditional patentability and prosecution rules, which suggests that the INPI might have influenced Anvisa. Interestingly, Anvisa issued consents with PGOs without any opportunity for applicants to explain or amend the application (see Appendix A), which happened before the INPI issued the rejections. Despite this difference, their citation rates were similar, which might indicate the consistency of the examination standard to which both entities unintentionally converged.

All 258 second decisions from the INPI analysed in this chapter happened after Anvisa also gave a negative decision, as defined in Section 3.2.2. Comparing these applications, the entities cited the same grounds for 25, assessed as total agreement, and different grounds for 233, or partial agreements. Figure 3.4 presents how frequently the entities cited each group of articles when in partial or total agreement. Prosecution rules and exclusions were cited more frequently when they were in total agreement (40.8% and 32.6% versus 36.0% and 16.0%) while traditional patentability was cited more frequently in partial agreements (72.0% versus 66.5%). Curiously, invention description was cited as often in partial and total agreements.

Figure 3.4. Citation rate of groups of articles for applications with negative decisions from both entities where there was partial or total agreement on the grounds



In addition, the average number of articles cited by the entities was estimated. As the first to decide, the INPI cited, on average, 2.1 articles per negative decision in the first period, and Anvisa cited 2.8 articles in the second and 3.4 in the third. As the second to decide, the INPI cited 3.1 in the third period and Anvisa 1.6 in the first. The increase in averages over time indicates a convergence to higher citation patterns. It makes sense that Anvisa cited fewer articles than the INPI as second to decide because it only examined applications the INPI intended to grant. The same does not apply in the third period since most of Anvisa's decisions were non-binding consents with PGOs, so the INPI still had to examine the applications.

Finally, the diversity of decisions was analysed as in the number of groups of articles cited. In the first period, 48.1% of the INPI's negative decisions cited multiple groups, a figure which grew to 78.3% in the third period. Meanwhile, Anvisa's share of multigroup decisions grew from 67.6% in the second period to 83.4% in the third. Thus, both entities became more diverse in the cited grounds, with Anvisa's decisions slightly broader than the INPI's in the third period. Thus, Anvisa tended to issue broader decisions than the INPI, but both entities converged to a pattern of high frequency and diversity of grounds cited.

3.4 Discussion

The first main finding of this investigation is that, even though both entities were considering the same articles of the LPI while examining pharmaceutical patent applications, the INPI as first to decide tended to focus on the traditional patentability criteria as grounds for negative decisions. Meanwhile, Anvisa seemed to be less focused, also finding other criteria highly relevant, especially invention description. This finding for the two decades of dual examination is consistent with what Silva (2008) found when analysing Anvisa's decisions in the early 2000s, shortly after this system was introduced.

As indicated in Section 3.3, there are possible explanations for the differences in citation rates. As the health regulator, Anvisa might have been more interested in excluding health-related methods or parts of living organisms from patenting. In addition, the *sui generis* selection process (see Appendix A) required that Anvisa think more carefully about which products might be related to the invention, making it more likely to cite issues with the description. Due to this higher scrutiny of the description, Anvisa might also have noticed issues with prosecution aspects such as improper amendments or multiple applications covering the same inventive concept. Lastly, some argue that the results are influenced by Anvisa targeting specific types of applications, especially secondary inventions (Shadlen 2011; 2017; Guimarães and Corrêa 2012; Correa 2014; Sampat and Shadlen 2015; 2017).

This chapter cannot confirm the validity of these explanations because it did not analyse the type of invention. Future studies should investigate if the entities disagreed more often on primary or secondary inventions. If Anvisa targeted secondary inventions, the citation pattern for primary inventions should be closer to that of the INPI. Alternatively, disagreements could be more frequent for primary inventions if, instead of specific inventions, Anvisa applied a higher level of scrutiny to all pharmaceutical applications. Similarly, studies focusing on applications with negative decisions from Anvisa citing pharmaceutical exclusions but not from the INPI could investigate the prosecution history to understand why they disagreed.

The other main finding was that both entities converged over time to a pattern of higher and more diverse citation rates. The INPI's negative decisions after the 2017 Joint Ordinance were closer to Anvisa's in that period than the INPI's own decisions before 2013. Since the substantial changes were in the groups of articles that Anvisa cited much more frequently, this seems to be Anvisa's direct and indirect influence. Direct, because the INPI was examining applications with PGOs from Anvisa. Indirect, because of the history of interactions between

the entities. Sampat and Shadlen (2015; 2017) had already opined that the INPI, as the first to examine, could have anticipated Anvisa's denial of consent and cited articles it would have otherwise ignored. This chapter builds on that suggestion, providing evidence of new and cumulative avenues for influence.

The most significant result of this influence between the entities was invention description being cited much more often, especially by the INPI. The patent rationale consists of an equilibrium between the private incentives with temporary exclusivity and the public incentives with public knowledge disclosure (Macdonald 2002; Granstrand 2005; Andersen 2006; Rockett 2010). Therefore, the higher relevance given to this aspect is consistent with the special attention that many authors have paid to the role of information in the patent mechanism. Information is the product and a key input of inventive activity (Arrow 1962), so the effectiveness of patents depends on how well the invention is described in the application (Teece 1986). Since patents do not cover uncodifiable or tacit knowledge, inventors may withhold the knowledge that they cannot or need not describe to make copying the invention harder (Cohen and Levinthal 1989; Cowan, David and Foray 2000). Guaranteeing that inventions are sufficiently described is thus essential to promoting balance stimuli in patenting.

Although not the focus of this chapter, there is evidence of Anvisa's influence on the outcome. The INPI reverted its intention to grant 36 applications in the first period after Anvisa requested explanations or amendments to applications. This is especially interesting because it means the INPI recognised an error in its previous examination at a time when it argued that Anvisa's involvement was not necessary. Thus, even when the INPI was not open to cooperating with Anvisa, there were at least 36 cases where it benefitted from the second examination. Overall, consent was denied to 183 applications that the INPI intended to grant, representing 11.9% of applications Anvisa examined after the INPI. Lastly, 387 applications were abandoned after Anvisa issued a negative decision. This might not have been the deciding factor in all cases, but it is reasonable to assume it played some part.

It has been suggested that another significant contribution from Anvisa would be reducing the scope of granted patents (Silva 2008; Sampat and Shadlen 2015; 2017). Citing Anvisa's reports, Guimarães (2019) claimed that 36.6% of applications given consent by 2008 had been altered at its request. As explained in Subsection 3.2.1, the focus on negative decisions does not allow for an analysis of how much Anvisa influenced the reduction of claims. Future studies should compare the influence of examiners from Anvisa and the INPI on the changes

from the original applications to the granted patents to investigate how one entity might have influenced the other's requests and how responsive applicants were to each entity.

The dual examination mechanism appears to be an effective strategy to strengthen pharmaceutical patent examination. Because of it, applications are scrutinised more attentively, considering all the different rules in the patent law beyond the three traditional criteria of novelty, inventiveness, and industrial applicability. It also brought attention to other criteria. To invention description, perhaps because of its *sui generis* selection process that requires it to identify the products and therapeutic uses related to the invention. To health-related exclusions, as one might expect from the health authority. And to improper amendments to the application which might become more obvious once inventions are better described.

The choice to implement this mechanism depends primarily on human and financial resource availability and is influenced by the development stage. Patent offices are significantly worse resourced, and there is greater asymmetry in access to the judicial system in developing countries than in developed countries. If lax examination and the subsequent granting of low-quality patents compromises the balance between private and public stimuli of the patent system, preventive (*ex ante*) and corrective (*ex post*) measures must be employed. Especially for developing countries, the literature recommends focusing on the former (Drahos 2008; 2010; Hemphill and Sampat 2012; Shadlen 2013; 2017). In that sense, dual examination might be a useful strategy to promote balanced stimuli under TRIPS by making examination more rigorous. This strategy becomes even more relevant in response to continuous proposals in recent free-trade agreements to go beyond TRIPS (Correa 2000; 2014; 2022; Deere 2009; t' Hoen et al. 2018; Shadlen 2017; Shadlen et al. 2020; Tenni et al. 2022).

It matters how this policy is implemented given the complexity of its operation, as explained in Section 3.1, particularly when there is no *a priori* clarification on why it was introduced and how it should work. Even after two decades of learning by doing, the entities were more capable of determining what was excluded from the system than included (see Appendix A). The two decades of this policy were marked by intense debate over Anvisa having the power to stop the INPI from granting a patent, but it was common ground that non-binding PGOs could be submitted and are compliant with TRIPS (Barbosa 2006; Basso 2006; Barbosa 2018; Di Blasi 2019).

Analysing the first decade of the dual examination system based on the taxonomy of stability and enforcement of institutions created by Levitsky and Murillo (2009), Shadlen (2011) showed how the dual examination mechanism was being progressively weakened. The continuous challenges in the judicial, political and bureaucratic arenas seriously undermined the stability of the policy, and the INPI would leave applications in limbo after Anvisa denied consent, refusing to accept that another entity had the power to issue binding decisions on patentability. This process of weakening Anvisa's role continued beyond the period examined by Shadlen, with the INPI not accepting consent denials, the court orders forcing Anvisa to give consent, and full examination being restricted to applications related to SUS. However, even in the most conflictual period, there were many cases where the INPI agreed with Anvisa, changing its decision to a rejection, proving that this policy could be mutually beneficial.

Paradoxically, one may argue that the weakening of this policy was precisely what made the 2017 Joint Ordinance possible. It resulted in Anvisa agreeing to consider all articles of the LPI only when related to SUS, to deny consent based solely on banned substances, and to submit other objections in non-binding PGOs. The INPI agreed to end the prosecution by declaring applications forcibly abandoned when Anvisa denied consent and to consider Anvisa's PGOs when re-examining the applications. Also, the PGOs being non-binding led applicants to stop filing for court orders to force Anvisa's consent. Thus, the policy's enforcement and stability increased considerably when its scope was reduced and defined, leading to a virtuous process of influence and convergence. As such, Anvisa's prior consent exemplifies how institutional weakening can be reversed, producing a new, stronger policy instead of simply trying to preserve the original policy design.

Since this policy had become almost symbiotic, one might wonder why it was abolished in August 2021. Barbosa et al. (2024) reviewed the political and judicial movements that led to the extinction. The most important aspect is that the directory of Anvisa supported the end of the mechanism as long as the submission of non-binding PGO was included in its governing law as a regular duty of the entity.

The dual examination system was initially weakened by the lack of clear rules, which encouraged challenges from all fronts, but when the entities agreed on how to share responsibilities, it became a strong instrument to promote patent examination rigour, with one entity influencing the other and both converging to higher standards. Based on the results of this chapter, it makes sense that Anvisa would agree to revoke the article of the LPI if the

submission of PGOs was guaranteed in its governing law. That was its main mechanism of influence, and the denial of consent based on banned substances was largely irrelevant. It should have reduced the criticism and allowed for better management of limited resources. However, that is not what happened. With the dual examination mechanism being abolished, Anvisa can submit non-binding PGOs, but only when requested by the MoH.

3.5 Conclusion

The main findings of this investigation of the dual examination mechanism in Brazil between 2001 and 2021 are that the patent office and the health regulator used to differ greatly on the grounds for their negative decisions. Initially, the INPI focused on traditional patentability, while Anvisa had a more diverse approach and cited invention description most often. Over time, both entities converged to higher citation rates, suggesting one influenced the other, especially with the INPI's decisions becoming closer to Anvisa's than its past decisions. The higher relevance given to invention description is consistent with the goal of balancing the private and public incentives in the patent system. There is also evidence of Anvisa's influence over the outcome and of the INPI benefitting from Anvisa's decisions even as it rejected any form of cooperation. Thus, this mechanism significantly elevated the standards for granting pharmaceutical patents in Brazil.

The lack of clarity about why and how this mechanism should work led to its continuous weakening through administrative conflicts between the entities and an intense legal and political debate. Nonetheless, this weakening probably created the conditions for both entities to agree on a more reduced version of the mechanism, with clearer rules, which created an almost symbiotic process where most of the influence was done through non-binding opinions. The lesson here is not to maintain a poorly defined policy until it becomes a stronger version but to understand that something like the dual examination system works best when rules are clearly defined and the entities are willing to cooperate.

Future studies should investigate why the mechanism was abolished when it was finally working well and why the submission of non-binding PGOs for strategic applications has not yet been formally declared one of Anvisa's key roles. Anvisa examiners interviewed for this thesis explained that the division responsible for this task was reduced to less than a handful of people and they depend on the MoH selecting relevant applications and requesting the examination of patentability criteria. When there are issues, they send the PGOs to the MoH,

which then decides if these will be submitted to the INPI. In that case, the MoH should be proactive in requesting Anvisa's opinion on the patentability of strategic pharmaceutical applications and should always submit the resulting PGOs to the INPI.

The Brazilian experience of dual examination of pharmaceutical patent applications can provide crucial lessons for the TRIPS flexibilities debate. This policy has precedent in Brazil and has been at least proposed in many countries. It is a proposal for cooperation to make patent examination more rigorous. As a multi-entity policy, this strategy requires careful design, but Brazil has shown it can be done in less conflictual and more mutually beneficial ways.

4 INDUCING COMPETITION IN PHARMACEUTICAL TENDERS: CENTRALISED PROCUREMENT OF HEPATITIS C DRUGS IN BRAZIL

Historically, most countries have imposed some restrictions on the patenting of pharmaceutical products as a strategy to promote access to medicines and develop national industries (Chang 2001; May and Sell 2006; Orsi & Coriat 2006; Deere 2009). However, countries had to give up the power to exclude certain industries after signing the TRIPS Agreement in 1994 which was a condition of joining the newly created WTO. But patents are not a binary mechanism, where their presence or absence leads to full or no exclusivity. Patents may not create monopolies if the product is not covered (e.g., a patent on the manufacturing process) since competitors may develop alternative ways to manufacture the product that circumvent the protection. Even if the product is protected, alternative treatments might create possibilities for competition. Thus, the effect of patents on pharmaceutical competition depends on the strength, scope and duration of the protection and is influenced by factors like therapeutic substitutability.

This chapter focuses on the centralised procurement of drugs[47] to investigate the real-world effects of the interplay between patent exclusivity and therapeutic substitutability. It analyses when the government may induce competition by forcing the original manufacturers of different products, known as 'originators', to compete among themselves and sometimes even with manufacturers of generic versions. This analysis draws from the empirical literature on pharmaceutical tendering strategies (Maniadakis et al. 2018; Wouters et al. 2019; Parmaksiz et al. 2022; Barrenho et al. 2023).

Brazil's experience of treating patients with the HCV provides a useful case for analysing these dynamics. One of the leading causes of viral hepatitis, HCV is transmitted via direct contact with infected blood, normally by sharing needles or syringes, with two-thirds of patients developing chronic infections which may result in cirrhosis, liver cancer and possibly death. Comparing estimates by the World Health Organisation (WHO) for 2017 and 2022, the annual global number of new HCV infections has fallen from 1.75 to 0.98 million, and deaths have fallen from 400 to 244 thousand (WHO 2017; 2024b).

Given this sizeable public health challenge, the introduction of direct-acting antiviral (DAA) drugs represented a revolution in HCV treatment (Mathur et al. 2018; Lobato et al.

[47] In this chapter, a 'drug' is an active pharmaceutical ingredient, a 'product' is a version of a drug manufactured for marketing, and a 'regimen' is a unit of treatment.

2019; Zoratti et al. 2020; Sulkowski et al. 2021). Before them, there was only one standard treatment that was very long and had a low cure rate, with frequent and serious side effects. Since first introduced in 2013, there have been three generations of DAA drugs that allow for much quicker and simpler treatments with very high cure rates and fewer side effects. Also, there are a few highly effective treatments, increasing access and the likelihood of success.

The advances in treatments have been accompanied by substantial controversy around DAA drugs, especially sofosbuvir. When introduced in 2014, it became the most expensive pill on the market, creating significant financial pressure even for rich countries. Questions about its patentability also led to many disputes at patent offices and courts worldwide between the originator, Gilead, and other originators, generic manufacturers and civil society organisations (Douglass et al. 2018; Bourgeon and Geiger 2021). This controversy was fuelled by the volume of public support that went into the development of sofosbuvir (Barenie et al. 2021) and by this being the most important drug for HCV, included in many combination treatments. In response, Gilead issued voluntary licences for Indian generic manufacturers to manufacture and sell the drug to developing countries. However, opposition remained strong in countries that were not included, leading to many applications being rejected, patents being granted with reduced claims, and Malaysia even issuing a compulsory licence, to which Gilead responded by extending the voluntary licences to Malaysia and a few other countries (Douglass et al. 2018).

Brazil is also an interesting case study because it is one of the middle-income countries with a high incidence of HCV not covered by Gilead's voluntary licensing agreements (Douglass et al., 2018). It has played a leading role in raising global awareness about viral hepatitis, proposing the first WHO resolution on this disease, which created World Hepatitis Day in 2010, and co-sponsoring the 2014 resolution calling for effective strategies to combat the illness. It also joined the UN's Sustainable Development Goal of eliminating this global health threat by 2030 and vowed to cure any Brazilian resident infected by HCV (WHS 2017). However, the performance in case detection and treatment has been significantly below the MoH's estimations of what would be necessary to treat the estimated 632,000 Brazilians infected with HCV in 2019, putting this 2030 goal in question (Benzaken et al. 2019; MoH 2024a). The 1988 Brazilian Constitution also guarantees universal access to healthcare through SUS, forcing the government to optimise expenditure in procurement and provision of treatment, often via centralised procurement (Chaves et al. 2017; Arantes and Fonseca 2022).

This chapter combines primary and secondary data in a mixed-methods case study of centralised public procurement of HCV drugs in Brazil. The research aim is to understand how patent exclusivity and therapeutic substitutability affect the government's bargaining power by analysing the negotiation in centralised procurement. For that, it needs to understand the conditions for competition based on which alternative treatments were recommended by the MoH since 2015 and how they have differed in effectiveness, which originator and generic products have been approved by Anvisa and were available in the market, and the level of patent exclusivity of each drug. Combining these three dimensions into timelines from 2015, it investigates what led to the discontinuation of some products and the registration of some generic versions. After understanding which versions of the treatments were available on the Brazilian market, it analyses the centralised procurement history to understand which products were bought and how the actors negotiated. Lastly, it designs a matrix of competition scenarios to discuss the effects of patent exclusivity and therapeutic substitutability on the government's bargaining power, comparing the findings with the empirical literature on pharmaceutical tendering and other policies to reduce drug prices.

The findings show that the government could induce competition because the newer DAA-based regimens were considered highly comparable in effectiveness, allowing it to buy the cheapest option. The competition was further increased due to unexpected gaps in patent exclusivity when patentees abandoned their patents or when the rigorous and contentious prosecution system resulted in minimal effective exclusivity. Having originators and generic manufacturers compete in tenders effectively increased the bargaining power and reduced the prices of drugs even more than in previous centralised purchases via individual negotiations. Therefore, this case study illustrates the potential benefits and shortcomings of pharmaceutical tendering drawn from the empirical literature, which also opens avenues for future studies.

Discussing the results, this chapter finds that the incentives to local production helped this strategy by promoting the launch of generic alternatives but only when commercially interesting, based on the MoH's guidelines, and viable under the respective patent exclusivity. Also, the discounts were so significant that contracts were negotiated well below the price caps set by Anvisa, making the price control policy not affect centralised procurement. Yet, the positive effects were limited by market concentration when drugs were removed from the guidelines, discontinued by manufacturers, or when suitable competitors refused to place offers. Thus, the government should explore the possibility of inducing competition more often,

invest in developing local productive capabilities and making tenders more attractive, and revise its price regulation policies.

This chapter is divided into seven sections. One is dedicated to the data on treatment guidelines, another to market approvals, and a third to patent landscapes. Then, these data are combined into timelines for each drug since 2015 to explain why some products have been discontinued and why only two drugs have generic products in Brazil. Next, the procurement history is analysed, focusing on the tenders. Lastly, the matrix of competition scenarios is presented to discuss the pros and cons of the strategy of inducing competition, drawing from the literature on patent exclusivity, drug prices and public procurement.

4.1 The history of HCV treatment in Brazil

After the HCV genome was sequenced, Brazil introduced the newly developed specific tests in 1993 and made the notification of diagnosis compulsory in 1999 (MoH 2015; Coutinho et al. 2021). In 2000, the MoH published the first Clinical Protocol and Therapeutic Guidelines for Hepatitis C and Coinfections. In 2002, it created the National Programme for the Control of Viral Hepatitis, integrated into the Department of Sexually Transmitted Diseases, Aids and Viral Hepatitis in 2009. Despite the MoH centralising HCV drug procurement since 2006, these drugs may also be purchased privately or publicly, including when mandated by court decisions (Chaves et al. 2017; Arantes and Fonseca 2022).[48]

To be in the guidelines, drugs must first be approved for marketing by Anvisa and included in the SUS system by the MoH's National Committee for Technology Incorporation (CONITEC). Over time, several drugs have joined and left the guidelines, some recommended only for special cases or for managing side effects (MoH 2011; 2015; 2017; 2019). Before 2013, the sole regimen was pegylated interferon 2a and 2b with ribavirin. Since then, the MoH has periodically updated the list to include the most effective DAA-based treatments but it also includes non-DAA drugs that are used for managing side effects or treating special cases.

Based on the list of drugs, the MoH updated the treatment coverage and procurement rationale. When the first DAAs were introduced in 2013, treatment was limited to severe cases

[48] Patients often seek court mandates for the government to buy specific treatments, especially when they are too costly or still in experimental stages, generating several small purchases. Thus, prices tend to be much higher than in centralised procurement (Wang 2008; Lamprea 2017; Caetano et al. 2022). In 2016, these purchases represented 7% of public expenditure on drugs, with sofosbuvir having one of the highest shares (Vieira 2020).

due to the lack of experience with these drugs and budget restrictions. The MoH also directed that purchases should be based on cost-effectiveness since the regimens produced different results. In 2017, the MoH extended treatment to moderate cases based on better results with newer treatments and the commitment to the 2030 goal of ending HCV as a public health threat.

The most important change happened in 2019 when the MoH declared the regimens were highly effective and 'absolutely comparable', leading it to make treatment universally accessible and change the procurement rationale to cost minimisation (MoH 2019, p. 41). This understanding is in line with the recommendations from the WHO and the evidence from many clinical studies (Mathur et al. 2018; Lobato et al. 2019; Zoratti et al. 2020; Sulkowski et al. 2021). Thus, the government could simply buy the cheapest option for similar cases.

Another important change happened in 2022. The MoH issued a directive restricting future purchases to the three pangenotypic DAAs recommended by the WHO: sofosbuvir+daclatasvir, glecaprevir/pibrentasvir and velpatasvir/sofosbuvir (MoH 2022a; WHO 2024b).[49] Pangenotypic regimens can be given to patients with similar conditions independent of the HCV genotype, skipping the preliminary testing stage, which means treatment is cheaper, simpler and faster (Zoratti et al. 2020). Still, the MoH declared that the stock of ledipasvir/sofosbuvir should still be used to avoid waste. A new directive in 2023 defined the first line of treatment as sofosbuvir+daclatasvir or velpatasvir/sofosbuvir, with sofosbuvir+glecaprevir/pibrentasvir as an option for cases of therapeutic failure (MoH 2023).

Based on the updates to the guidelines and directives since 2015, Table 4.1 lists the recommended DAA-based regimens and briefly characterises the treatments. Regimens are compared for patients without other infections or a previous DAA treatment. This case study is focused on DAA-based regimens recommended since 2015 because they revolutionised HCV treatment by making it quicker and increasing the cure rate significantly (MoH 2015; Mathur et al. 2018; Lobato et al. 2019; Zoratti et al. 2020; Sulkowski et al. 2021). Moreover, interferon is not necessary, and ribavirin is only used for complicated cases, significantly reducing the side effects. Thus, this study focuses on the standard DAA-based treatment of adults without coinfections and who have never taken DAA drugs before.

[49] A plus sign indicates that a unit of treatment with sofosbuvir+simeprevir consists of one tablet of each drug. Meanwhile, elbasvir/grazoprevir is a single-table regimen, indicated with a slash. Regimens can have both combination types, as with the veruprevir/ritonavir/ombitasvir+dasabuvir (3D) regimen.

Table 4.1. List of HCV treatment regimens using DAA drugs in Brazil since 2015

Regimens	Concentration	Form	Treatment		Guidelines*				
			Daily dose	Duration (weeks)	2015	2017	2019	2022	2023
elbasvir/grazoprevir	50mg/100mg	Tablet	1	16			X		
glecaprevir/pibrentasvir	100mg/40mg	Tablet	1	8			X	X	
ledipasvir/sofosbuvir	90mg/400mg	Tablet	1	12			X		
sofosbuvir+daclatasvir	400mg+60mg	Tablets	1+1	12	X	X	X	X	X
sofosbuvir+simeprevir	400mg+150mg	Tablets	1+1	12	X	X			
sofosbuvir+glecaprevir/pibrentasvir	400mg+100mg/40mg	Tablets	1+1	12					X
velpatasvir/sofosbuvir	100mg/400mg	Tablet	1	12			X	X	X
veruprevir/ritonavir/ombitasvir +dasabuvir	75mg/50mg/12.5mg +250mg	Tablets	2+2	12		X			

Note: Considering the 2022 and 2023 directives that changed treatment recommendations (MoH 2022a; 2023b).

4.2 Products registered in Brazil for HCV treatment

Anvisa has multiple roles in the regulation of the Brazilian pharmaceutical market, from clinical trials to the surveillance of products. This study focuses on the marketing authorisation of products based on quality, safety, and efficacy. There were 15 such products connected to HCV drugs in Anvisa's database, from which data was extracted about the product name, the type of product, who registered it and when, and the discontinuation date (Anvisa 2024).[50]

While most of the variables in Table 2 are self-explanatory, it is important to define the types of synthetic products.[51] 'Originator' products are new molecules registered for the first time in Brazil. 'Generic' products are identical versions of molecules already registered for a specific therapeutic use, with equal bioequivalence and bioavailability, that cannot have a brand name and must be at least 35% cheaper than the respective new products. 'Branded generic' products have the same technical requirements of bioequivalence and bioavailability as regular generics but may have brand names, exempting them from the mandatory discount.

Unsurprisingly, all originator products have been approved since the drugs must be registered with Anvisa to qualify for incorporation into SUS. Alternative versions have also been approved for two drugs, which may seem surprising because many countries only allow the registration of alternatives once there is no effective patent exclusivity (Son et al. 2018;

[50] Approvals are valid for 10 years and may be renewed. Due to commercial strategies or manufacturing conditions, products may be discontinued temporarily or definitively. This study considered the definitive discontinuations when the MoH published the decision in the Union's Official Gazette.

[51] In Anvisa's terms, the three categories are called 'new', 'generic', and 'similar', respectively (Anvisa 2022c).

Raju 2022). However, Brazil allows the registration of generics before the end of the patent protection period to avoid delaying their launch.

Table 4.2. Products for HCV treatment with marketing authorisation by Anvisa

Product	Drugs	Lab	Type	Production	Registered	Discontinued
Daklinza	DCV	BMS	Originator	Imported	06/01/2015	11/12/2020
daclatasvir dihydrochloride	DCV	Blanver	Generic	Imported	05/12/2022	
daclatasvir dihydrochloride	DCV	Fiocruz	Generic	Imported	26/02/2024	
Zepatier	ELB/GRA	MSD	Originator	Imported	04/12/2017	30/09/2022
Maviret	GLE/PIB	AbbVie	Originator	Imported	16/04/2018	
Harvoni	LED/SOF	Gilead	Originator	Imported	04/12/2017	
Olysio	SIM	J&J	Originator	Imported	11/03/2015	17/01/2019
Sovaldi	SOF	Gilead	Originator	Imported	30/03/2015	
sofosbuvir	SOF	Blanver	Generic	Local	21/05/2018	
sofosbuvir	SOF	Fiocruz	Generic	Local	02/07/2018	
Sophir	SOF	Blanver	Branded generic	Local	29/04/2019	13/05/2021
sofosbuvir	SOF	EMS	Generic	Local	23/11/2020	
sofosbuvir	SOF	Furp	Generic	Local	29/03/2021	
Epclusa	VEL/SOF	Gilead	Originator	Imported	25/06/2018	
Viekira	3D	AbbVie	Originator	Imported	22/04/2015	20/02/2020

Note: Acronyms are used for drug names: daclatasvir (DCV), elbasvir (ELB), ledipasvir (LED), glecaprevir (GLE), grazoprevir (GRA), pibrentasvir (PIB), sofosbuvir (SOF), and velpatasvir (VEL). The acronym 3D is used for veruprevir/ritonavir/ombitasvir+dasabuvir.

All generics are involved in the Productive Development Partnerships (PDP) in which the government promises a share of its purchases for a private firm that voluntarily licences a strategic technology, promoting local production by national public laboratories. Sometimes, there are two private partners: an international firm transferring the technology and a national firm receiving it while helping the public laboratory internalise it. A national pharmochemical firm often internalises the active pharmaceutical ingredient (Pimentel 2018; MoH 2024b). All members of the PDP need to register their versions. For example, the PDP between Blanver and the Oswaldo Cruz Foundation (Fiocruz) generated two versions of daclatasvir and two of sofosbuvir,[52] and the PDP between EMS and the Popular Medicine Foundation (Furp) resulted in two versions of sofosbuvir.[53] Other PDPs have been proposed but never signed or were abolished before the transfer was finalised (Cassier and Correa 2019; MoH 2024b).[54]

Since Anvisa may approve a generic version while the drug is still patented, one cannot infer the patent status from the approved products. Still, the patent status might have influenced

[52] Both PDPs involved the pharmochemical firm Microbiológica. The daclatasvir PDP also involved an Egyptian company, Pharco, which transferred the technology to both Blanver and Fiocruz. Since this transfer is still happening, the versions that both firms have registered are still manufactured by Pharco in Egypt.
[53] This PDP also included the pharmochemical firm Globe.
[54] There was a PDP for sofosbuvir involving Gilead, but some have suggested that Gilead was trying to block the other PDPs in case no patent was granted, which it also did judicially (Cassier and Correa 2019; Achcar and Fonseca 2024). All sofosbuvir PDPs were suspended by the MoH in 2018 despite the patents not blocking generic manufacturing (see Section 4.4). Blanver's PDP was reinstated in November 2023, and EMS's in January 2024.

the registration of generic versions for only two drugs or the discontinuation of four originator products and the branded generic sofosbuvir. To investigate this, Section 4.3 is dedicated to mapping each drug's patent landscape and Section 4.4 builds a timeline combining treatment guidelines, marketing approvals and patent protection to investigate the circumstances behind the discontinuations and generic registration.

4.3 The Brazilian patent landscape of HCV drugs

This section searches for the patent applications in Brazil that cover the drugs used for HCV treatment to identify the level and period of protection. This type of patent landscaping analysis is complicated by the fact that a single drug may be protected by multiple patents (e.g. alternative molecular forms), and a single patent may cover multiple drugs (e.g. different combinations). Moreover, it may not be clear from the description of the invention in the application which products it relates to. As a result, this tends to be a costly and time-consuming investigation (Trippe 2015). As an alternative to reading thousands of documents, this study turned to databases that match drugs and applications, along with previous landscaping reports on HCV drugs. The focus was on applications covering the drugs and the combinations listed in the guidelines, ignoring combinations not recommended or used for different treatments.[55]

Unfortunately, there is no central registry in Brazil connecting patent applications and drugs.[56] Instead, data was extracted from multiple sources: the United States Food and Drug Administration's Orange Book (FDA 2023), which connects approved drugs and some granted patents;[57] the Medicines Patent Pool's Medicines Patent and Licence (MedsPaL) database, which lists key applications for a selected group of drugs (MPP 2023); HCV patent landscapes published by international agencies (WHO 2016; UNITAID 2015a; 2015b; 2017a; 2017b; 2017c); and the MoH's requests for the INPI to fast-track specific patent applications related to HCV drugs (INPI 2019f). Given the methodological differences between the sources, any application they listed was included if it covered the drugs or their recommended combinations.

[55] Ritonavir is an old drug first approved and patented for other uses, and there was no pending or valid compound patent when the 3D regimen was introduced (INPI 2019e). Thus, the applications included cover ritonavir as part of 3D, not the drug itself.

[56] Originators must indicate a patent application filed in Brazil. These data were requested via the Access to Information Law, but Anvisa said that it does not have a structured database and the documents are confidential.

[57] The Orange Book only lists granted patents that cover the compounds of synthetic drugs, their indications, or methods of use. Also, it is self-reported by manufacturers without verification by the FDA (Durvasula et al. 2023).

These applications were used to define the relevant patent 'families'. Patents are territorial, so applicants must file separately in each jurisdiction where they seek to protect an invention. Patent families group these separate applications covering the same inventive concept. In November 2024, data on Brazilian applications related to these families were extracted from the INPI's Buscaweb database, checking if any had been split (INPI 2024f). Applications in Brazil may be split, keeping the reduced original application and replacing certain aspects in 'divisionals', which inherit the prosecution history of the original. Examiners might request a split if the application contains multiple inventive concepts, and applicants might want to split applications to place the controversial claims in divisionals, file follow-on applications on secondary aspects, or make it harder for competitors to keep gauge and challenge the protection scope (Minn 2016). Applications cannot be split after the grant or rejection is published, and divisionals cannot be split again.

Next, eight aspects of the prosecution history of the 89 Brazilian applications were analysed: a) the outcome date; b) the granted patents' expiration dates; c) the applicants; d) if the prosecution was fast-tracked; e) if any third party submitted an opposition; f) if Anvisa denied consent or submitted an opposition; g) if the application was prosecuted under the Backlog Reduction Plan; h) if the applicant filed an appeal against the rejection or abandonment outcome; and i) if any party filed a lawsuit connected to the prosecution. Most of these categories are self-explanatory, but there are important things to keep in mind about Anvisa's opposition and the Backlog Reduction Plan.

Between 2001 and 2021, the INPI needed Anvisa's consent to grant pharmaceutical patents, as explained in Chapter 3. Until 2012, Anvisa re-examined the patentability of applications the INPI intended to grant. In 2013, Anvisa became the first to decide and only examined all patentability aspects of applications related to products offered via SUS. Otherwise, it simply screened them for banned substances. In 2017, Anvisa and the INPI signed an agreement wherein Anvisa could only deny consent due to banned substances but could still report issues with the patentability of strategic applications in non-binding oppositions.

Chapter 2 analysed the Backlog Reduction Plan, which the INPI introduced in 2018 as a strategy to expedite prosecution by simplifying the examination. The Plan works by adopting the prior art search report produced by other offices, mainly from the United States and Europe, to base the analysis of the novelty and inventiveness of the application. Assuming this reduces the amount of work that INPI examiners need to dedicate to each examination, the INPI also

pressured them to issue decisions faster. However, applications could not be prosecuted under the Plan if the examination had not been requested or had already started, if the application was under fast-tracking, or if Anvisa or any third party had submitted an opposition.

Table 4.3 summarises the data, with the detailed landscapes presented in Appendix B. Prosecution had ended for all applications except for two rejections pending an appeal. The outcomes were evenly distributed: 31.5% granted, 30.3% rejected, and 38.2% abandoned.[58]

Table 4.3. Prosecution history of patent applications related to HCV drugs in Brazil

Drug[1]	Applications[2]		Outcome			Opposition		Appeal	Litigation	Fast-track	Backlog Plan
	Total	Divisionals	Granted	Rejected	Abandoned	Anvisa	Others				
DCV	12	0	3[3]	2	7	5	1	0	0	8	0
DSV	7	0	1	1	5	1	0	0	0	0	2
ELB	3	0	1	0	2	0	0	0	0	0	1
GLE	9	0	3	3[4]	3	1	0	1	0	0	8
GRA	6	0	1	1	4	1	0	0	0	0	1
LED	9	2	5	0	4	4	0	1	0	5	1
OBV	5	0	2	0	3	0	0	0	0	0	3
PIB	9	0	3	3[4]	3	0	0	1	0	0	9
RTV	3	0	0	0	3	0	0	0	0	0	1
SIM	16	1	5[3]	3	8	9	0	0	0	10	0
SOF	27	11	5	16[4]	6	21	18	10	9	18	0
VEL	6	0	1	2[4]	3	2	1	2	1	2	2
VER	5	1	1	0	4	0	0	0	0	0	1

Note: (1) Acronyms are used for drug names: daclatasvir (DCV), dasabuvir (DSV), elbasvir (ELB), glecaprevir (GLE), grazoprevir (GRA), ledipasvir (LED), ombitasvir (OBV), pibrentasvir (PIB), ritonavir (RTV), simeprevir (SIM), sofosbuvir (SOF), velpatasvir (VEL) and veruprevir (VER). (2) Some applications covered multiple drugs, so the sum is bigger than the sample. (3) Applicants let all grants lapse. (4) One appeal to rejection is pending.

Anvisa opposed 41 applications and gave consent to 14. It issued no decision for the other 34 because the INPI never sent them (18), they were abandoned before it reached a decision (6), or the prior consent mechanism was abolished before Anvisa issued a decision (10). That a fifth of the applications were never sent to Anvisa is an example of the complexity in designing a selection process for what needed consent, as discussed in Chapter 3. Anvisa's opposition to 10 applications were originally consent denials, but court orders forced Anvisa to give it to eight, and the INPI considered the other two non-binding oppositions.[59]

Third parties also filed oppositions to 20 applications. In 11, multiple third parties opposed the grant, and in one of these cases, the opposition continued after the grant, with a third party requesting the nullity of the patent, but the INPI upheld the grant. Apart from these administrative actions, third parties filed lawsuits against four applications.

[58] The higher rate of abandonment than rejection is a historical trait of Brazil, as shown in Chapter 2.
[59] From 2017, the INPI considered previous consent denials not citing banned substances non-binding oppositions.

Meanwhile, applicants appealed 12 rejections and one abandonment[60] and filed lawsuits against Anvisa and the INPI regarding nine applications. Splitting applications was uncommon, except for sofosbuvir, which had six applications split, creating 11 divisionals.

Given the 2030 Plan to end HCV as a public health threat, it is surprising that the MoH only requested fast-tracking for 38 applications, restricted to daclatasvir, ledipasvir, simeprevir and sofosbuvir. Thus, this study provides evidence of the underuse of fast-tracking requests by the MoH.[61] There were two cases of fast-tracking requested by the same applicant, Gilead. One involved an application covering velpatasvir, which Gilead claimed an unauthorised third party was exploiting, and the other was for an application covering velpatasvir/sofosbuvir, which became fast-tracked in September 2024 because the INPI still has not decided on the appeal to the rejection despite it being filed in August 2020.[62]

The prosecution of 18 applications happened under the Backlog Reduction Plan. Applications were prosecuted outside of the Plan mainly because they were under fast-tracking and also because substantive examination had already started,[63] which explains why no daclatasvir, simeprevir or sofosbuvir application was under the Plan.

Finally, the outcome rates were compared based on the different prosecution elements. Rejections were more frequent when Anvisa and third parties submitted oppositions. When Anvisa opposed the grant, 34.2% of applications were granted, 56.1% were rejected, and 9.8% were abandoned. When it gave consent, 71.4% of applications were granted, and the rest were abandoned. When third parties filed oppositions, 20.0% of applications were granted, 75.0% were rejected, and 5.0% were abandoned. The rates for applications without third-party opposition were 34.8%, 17.4%, and 47.8%, respectively. Since the INPI always addressed these arguments in the decisions, it is reasonable to assume they had some influence. The results for Anvisa are in line with the findings in Chapter 3 about its influence on the INPI's decisions.

On the contrary, the INPI seemed less swayed by applicants' arguments in appeals to rejections. The INPI maintained the rejection in eight cases. It also maintained the abandonment after the applicant tried to re-split a divisional application. Only two appeals to rejections convinced the INPI to revert its decision. Lastly, two appeals are still pending.

[60] The unsuccessful appeal against an abandonment concerned an attempt to split a divisional.
[61] The Brazilian Supreme Court has urged the MoH to be more proactive in requesting fast-tracking (STF 2021).
[62] Fast-tracking was allowed via the specific program for health-related technology (INPI 2024g).
[63] In interviews for this thesis, specialists in the topic claimed that third parties strategically file oppositions to avoid applications being prosecuted under the Plan and that the MoH could use its fast-tracking requests similarly.

The main effect of fast-tracking on the outcomes was that applicants abandoned less often, which led to more rejections. In the end, 33.3% were granted, 43.6% were rejected, and 23.1% were abandoned.[64] Considering applications without fast-tracking, 30.0% were granted, 20.0% were rejected, and 50.0% were abandoned.

Finally, grants were a lot more frequent under the Plan than outside, and abandonments were much less frequent, in line with the findings in Chapter 2. When applications were prosecuted under the Plan, 55.6% were granted, 16.7% were rejected, and 27.8% were abandoned. Outside of the Plan, the rates were 25.4%, 33.8%, and 40.9%.

These comparisons should not be generalised, given the small sample size. Still, they illustrate general trends that are coherent with the findings in Chapter 2 about the Plan making the INPI grant a lot more often and in Chapter 3 about Anvisa influencing the INPI's decisions, promoting a higher examination standard.

4.4 The timelines of treatment guidelines, marketing approvals and patent protection

Based on these landscapes and the data on treatment guidelines and marketing approval, this chapter investigated what led to the registration of generic versions of just two drugs and the discontinuation of four originator products and the branded generic.

This analysis started by considering the periods of patent protection. While applications are pending, applicants have 'provisional rights' since they may claim retroactive compensation after the grant for any infringement during the prosecution. Although not under *de jure* exclusivity, inventions might have some *de facto* exclusivity in this period if launching alternative versions is risky (grant is likely) and costly (effective enforcement). If applications are successful, leading to patents being granted, applicants gain 'patent rights,' meaning *de jure* exclusivity. If applications are unsuccessful, i.e. rejected or abandoned, or when the patent term ends, inventions enter the 'public domain' and lose exclusivity. In that sense, there are three periods of protection: provisional rights if there was at least one pending application and no valid granted patent; patent rights if there was at least one valid granted patent; and public domain if there was no pending application or a valid granted patent.

[64] The application that was fast-tracked because of the INPI's delay in judging the appeal is still pending.

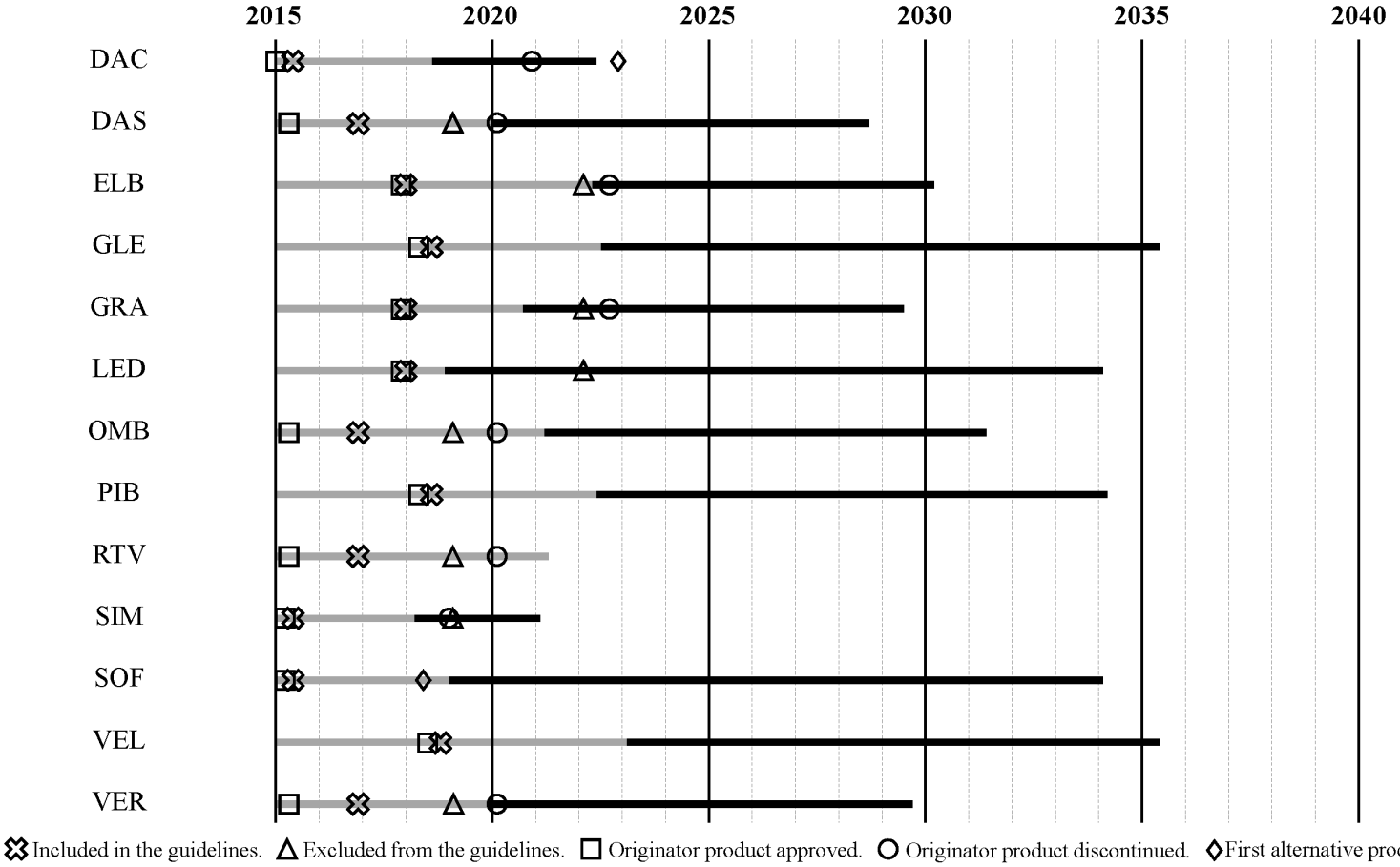
Considering the sample of 89 applications, Figure 4.1 illustrates the timeline for each drug, showing when it was recommended for treatment, when products were registered and discontinued, and the respective patent protection periods. These timelines illustrate the strategy of stacking applications to strengthen, enlarge and prolong protection, known as patent evergreening (Hemphill and Sampat 2012). Based on the filing dates of granted patents, these strategies will give five drugs more than 20 years of nominal protection: sofosbuvir (29.8 years), ledipasvir (23.7), glecaprevir (23.7), pibrentasvir (22.4), and ombitasvir (21.0). However, exclusivity is not homogeneous or guaranteed during these periods and depends on the scope and protection period of each patent. These periods might also be shortened if patentees stop paying post-grant maintenance fees, which happened with daclatasvir and simeprevir, shortening their protection periods to 14.8 and 16.1 years, respectively.

The timelines show a strong connection between approvals and guidelines: MSD, J&J and AbbVie discontinued Zepatier (elbasvir/grazoprevir), Olysio (simeprevir) and Viekira (veruprevir/ritonavir/ombitasvir+dasabuvir, or 3D) shortly after the drugs were removed. The MoH has removed ledipasvir/sofosbuvir but still recommended the use of remaining stocks, which explains why Gilead did not discontinue Harvoni.

However, the guidelines cannot explain the other two cases. Although daclatasvir is still a key drug, BMS discontinued Daklinza and let all patents lapse. This was a global decision to abandon the drug where it was not recommended or where it competed with alternative treatments (MPP 2020). Similarly, Blanver representatives interviewed for this thesis explained that it discontinued Sophir to focus on the generic version of sofosbuvir since the government would not buy the branded generic. Thus, changes to the guidelines and commercial strategies explain all discontinuations.

After that, the analysis turned to the registration of generic versions. The most straightforward case is daclatasvir. Blanver and Fiocruz registered their versions after BMS let all patents lapse, so there was no exclusivity despite the drug still being recommended. This differs from simeprevir since J&J let the patents lapse when its combination with sofosbuvir was removed from the guidelines. It makes sense that no generic was registered after the patents lapsed since the drug was no longer recommended. There were even two PDPs in early development, but they were cancelled.

Figure 4.1. The timelines of treatment recommendation, marketing approval and patent protection of HCV drugs in Brazil



Note: Acronyms are used for drug names: daclatasvir (DCV), dasabuvir (DSV), elbasvir (ELB), glecaprevir (GLE), grazoprevir (GRA), ledipasvir (LED), ombitasvir (OBV), pibrentasvir (PIB), ritonavir (RTV), simeprevir (SIM), sofosbuvir (SOF), velpatasvir (VEL) and veruprevir (VER).The timelines start in 2015 because that is this chapter's analysis period, but all drugs had at least one filing before that. The timelines indicate when drugs were included and excluded from the guidelines and when the originator and first generic products were approved by Anvisa and discontinued by the manufacturer. The timelines also illustrate the three periods of patent protection. In grey is the period of provisional rights, from the beginning of 2015 to the first grant or the last rejection or abandonment if no patent was granted. In black is the period of patent rights, from the first grant to the lapsing or expiration of the last granted patent. After that, lines stop to indicate the start of the public domain period.

The only other drug with alternative versions is sofosbuvir. There are four ways in which this is arguably the most controversial drug in the sample: the strategic use of divisionals, Anvisa's opposition, third-party opposition, and the applicant's defence strategies.

First, Gilead repeatedly split applications to separate controversial aspects and secure some exclusivity, especially for the two main applications. One covered the compound (PI0809654-6) and generated one divisional (PI0823519-8), but both were rejected. The other main application covered a chemical intermediate (PI0410846-9). It had 126 claims and was on track to be rejected, but Gilead split it, leaving only two claims. The INPI granted it and cited this grant as a reason to grant two divisionals (PI0419345-8 and BR122018015050-5). Gilead even tried to re-split one of the divisionals, but this is not allowed in Brazil.

Second, Anvisa opposed the grant of every sofosbuvir application it examined. It even denied consent to ten applications, but all were considered non-binding opinions because a court order forced Anvisa to give consent (8 cases) or because of the 2017 agreement between Anvisa and the INPI (2 cases). The INPI always considered Anvisa's opposition.

Third, other parties frequently submitted oppositions to sofosbuvir applications, as in other countries (Douglass et al. 2018; Bourgeon and Geiger 2021). These oppositions were explicitly considered by the INPI's and Anvisa's examiners in their decisions. The MoH requested fast-tracking for most applications, and the Brazilian Senate discussed a compulsory licence when the INPI decided to grant the chemical intermediate patent (Senado 2018).

Fourth, Gilead fought back, offering counterarguments to the opposition, litigating decisions from Anvisa and the INPI, and appealing negative outcomes. Gilead successfully secured the three grants despite Anvisa originally denying consent and reverted one rejection for sofosbuvir and another for ledipasvir/sofosbuvir. Yet, it could not revert the rejection of the compound patent, and an appeal to the rejection is pending for velpatasvir/sofosbuvir.

This extremely contentious process resulted in sofosbuvir itself not being under exclusivity. Gilead only obtained protection for a chemical intermediate and its uses, derivatives and formulations, and the combination with ledipasvir.[65] Thus, manufacturing generic versions of the drug was possible if using another intermediate, as claimed by generic manufacturers and confirmed by the government and the INPI in the Senate hearings and one

[65] The two grants for the ledipasvir/sofosbuvir combination were BR112014006324-9 and BR112014011938-4.

of the class actions against the grant of the first granted patent related to sofosbuvir (Fiocruz 2018; Senado 2018; Achcar and Fonseca 2024; Fernandes et al. 2024).

The other drugs without a compound patent in the analysis period were dasabuvir, ritonavir and velpatasvir. For the first two, one must consider that the 3D regimen consists of dasabuvir associated with ombitasvir, ritonavir, and veruprevir, so the full regimen was under exclusivity because of ombitasvir and veruprevir. For velpatasvir, the only granted patent covered production processes and intermediates (BR112016028773-8), and the application covering the velpatasvir/sofosbuvir combination (BR112016003644-1) had been rejected but is pending appeal. Generic manufacturers are likely waiting for this decision since Gilead could claim retroactive compensation for infringement if the appeal is successful and the patent is granted. If the rejection is confirmed and competitors can circumvent the single granted patent, the entire velpatasvir/sofosbuvir regimen will be in the public domain.

In conclusion, the combination of guidelines, patents and technology transfer policies explains why generics were only registered for daclatasvir and sofosbuvir. The former was in the public domain since the originator abandoned it for commercial purposes. Meanwhile, the intense opposition and litigation over the sofosbuvir applications resulted in exclusivity only for non-essential aspects. All other drugs were under some exclusivity or not recommended.[66]

4.5 Strategic public procurement of HCV products

This section analyses the centralised procurement history by the MoH since 2015 to identify how patent exclusivity and therapeutic substitutability influenced which drugs were bought and for how much. It draws on the data up to January 2024 from the Transparency Portal and the ComprasNet database, ignoring court-ordered purchases (Brazil 2024a; 2024b).

Table 4.4 summarises the procurement history, indicating the names and types of products, manufacturers, prices in Brazilian Reais (R$),[67] and treatment units. It separates tenders from direct negotiations and distinguishes between available products that were not purchased and unavailable products, i.e. not recommended or lacking marketing approval.

[66] Velpatasvir was under provisional rights based on the pending appeal to the rejection. Many were under exclusivity because of compound patents: elbasvir, glecaprevir, grazoprevir, ombitasvir, pibrentasvir, and veruprevir. Dasabuvir and ritonavir were in the public domain, but the regimen was under exclusivity because of the associated drugs. Finally, simeprevir was in the public domain but the regimen was no longer recommended.
[67] Updated using the Extended National Consumer Price Index to January 2024, when the last purchase happened (IBGE 2024). The average exchange rate for the United States dollar in that month was R$5.13 (BCB 2024).

Table 4.4. Treatment prices and units in procurement history (2015-2024, R$ constant)

Product	Drugs	Lab	Type		2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
Daklinza	DCV	BMS	Originator	$	12,143	10,057	9,183	9,047	-	-				
				N	21,834	30,317	10,460	14,760	-	-				
daclatasvir dihydrochloride	DCV	Blanver	Generic	$									-	-
				N									-	-
daclatasvir dihydrochloride	DCV	Fiocruz	Generic	$									4,398	-
				N									7,738	-
Zepatier	ELB/GRA	MSD	Originator	$					-	-	-			
				N					-	-	-			
Maviret	GLE/PIB	AbbVie	Originator	$					6,048	-	-	-	-	-
				N					25,118	-	-	-	-	-
Harvoni	LED/SOF	Gilead	Originator	$					*5,940*	*7,830*	-	-		
				N					*29,254*	*10,336*	-	-		
Olysio	SIM	J&J	Originator	$	12,455	10,013								
				N	8,772	5,076								
Sovaldi	SOF	Gilead	Originator	$	32,738	20,637	18,508	-	-	-	-	-	-	-
				N	31,956	35,056	12,715	-	-	-	-	-	-	-
sofosbuvir	SOF	Blanver	Generic	$				*3,616*	-	-	-	-	-	-
				N				*13,820*	-	-	-	-	-	-
sofosbuvir	SOF	Fiocruz	Generic	$				-	-	-	-	-	2,359	-
				N				-	-	-	-	-	7,738	-
Sophir	SOF	Blanver	Branded generic	$				-	-	-	-			
				N				-	-	-	-			
sofosbuvir	SOF	EMS	Generic	$							-	-	-	-
				N							-	-	-	-
sofosbuvir	SOF	Furp	Generic	$							-	-	-	2,329
				N							-	-	-	3,869
Epclusa	VEL/SOF	Gilead	Originator	$					*6,605*	*9,661*	*8,941*	*7,449*	*7,100*	-
				N					*12,028*	*7,763*	*7,439*	*9,333*	*7,292*	-
Viekira	3D	AbbVie	Originator	$			8,429	-						
				N			25,096	-						

Note: This table includes purchases until January 2024, with values updated to that month. It uses acronyms for drug names: daclatasvir (DCV), elbasvir (ELB), ledipasvir (LED), glecaprevir (GLE), grazoprevir (GRA), pibrentasvir (PIB), sofosbuvir (SOF), and velpatasvir (VEL). The acronym 3D is used for veruprevir/ritonavir/ombitasvir+dasabuvir. For each product, the top line indicates the price of a full treatment course negotiated, and the bottom line indicates the amount of treatment courses bought. Tenders are in italics; otherwise, direct negotiations. This table reports the year when purchase contracts were signed, which is not necessarily the same year of the tender in which the contract was negotiated. Blank spaces indicate when drugs were not recommended for treatment or lacked marketing approval. Dashes indicate that the drug was not purchased in that year even though it was recommended and had Anvisa's approval.

Before 2018, the MoH negotiated all contracts directly with the originators, obtaining yearly price reductions. Thus, the government had considerable bargaining power in those negotiations. Nonetheless, there has been an even more significant price reduction since 2018, when the government began to purchase via tenders.

Appendix C presents a summary of all the offers and the winners of each group per tender. Here, the tenders are summarised based on seven aspects of these processes. First, the MoH defines a maximum price for tenders, which should not be mistaken for Anvisa's price regulation. Second, each tender is separated into groups based on HCV genotypes and patients' conditions, so there may be multiple competitions and winners within the same tender.[68] Third, only products approved by Anvisa may be offered. Fourth, the manufacturer or distributors

[68] Tenders may designate a share of the group for micro and small businesses. Some tenders in this analysis had these special groups, but no such seller ever participated, so special groups are ignored.

may place offers, and they might compete. Fifth, the winning offer may be split into multiple contracts, with payment and delivery over a period and the possibility of adjusting quantities and prices. Sixth, any of the participants in the tender may file an appeal, which the auctioneer will examine after consulting with all participants and the MoH.[69] Seventh, all PDPs were suspended during the negotiation of the tenders in the sample, so there was no share of the procurement guaranteed for the transferors, which had to compete like any other seller.

The first tender (87/2018) was limited to sofosbuvir, with offers from Gilead and two distributors of Blanver's generic: Hospinova and Maxima. Gilead opposed any competition, claiming sofosbuvir was under patent exclusivity since the INPI had published an intention to grant the patent covering the intermediate and several others were still pending. Also, Gilead claimed that the maximum price was impossibly low, so the tender was unfulfillable and should be cancelled. Citing statements from the MoH and the INPI in a class action against the grant of the intermediate patent, Hospinova argued that the application covered a chemical intermediate not used by Blanver and that pending applications cannot forbid sales, or else provisional rights would be the same as patent rights. In other words, it assumed the risk of selling the generic because it could circumvent any protection sofosbuvir could obtain. Lastly, Hospinova and Blanver agreed to supply the drug at the maximum price as a one-off offer, given the urgency for HCV treatments. The auctioneer accepted Hospinova's arguments and denied the appeal, saving R$ 66.0 million (63%), compared with Gilead's best offer.

The second tender (105/2018) was the most competitive, including all regimens recommended at the time and with five manufacturers placing offers. Gilead won six groups, selling ledipasvir/sofosbuvir and velpatasvir/sofosbuvir. Instead of opposing Blanver's right to offer the generic sofosbuvir, Gilead's strategy was to focus on the combinations, offering them at a lower price than sofosbuvir alone, and giving aggressive discounts that defeated all competition. While Blanver and BMS gave significant discounts, their combined best offers were more expensive than Gilead's. AbbVie and MSD did not engage in this bidding war, placing offers at significantly higher prices. As a result, the MoH purchased treatments for six of the eight groups with a 52% discount on the maximum prices. No one won the other groups because all offers exceeded the maximum. A few months later, the MoH negotiated a contract directly with AbbVie for glecaprevir/pibrentasvir with an 80% discount on the best offer in the

[69] All documents related to the appeals are available on the ComprasNet database (Brazil 2024b).

tender. While the relationship between the tender and the contract is unclear, it is reasonable to believe that the former might have affected the latter.

The third tender (56/2020) included all regimens except for sofosbuvir+daclatasvir, but only Gilead joined, placing offers for ledipasvir/sofosbuvir and velpatasvir/sofosbuvir. It complained that the maximum prices had been estimated with an incorrect exchange rate, which has a significant effect since these products would be imported, and that the MoH increased the purchase volume after publishing the call, which Gilead said impacted the supply planning. Applying the correct rate, Gilead offered both drugs at 2% less than the previous tender in United States dollars. This meant they were 44% more expensive in Reais and above the maximum for the tender. Given the urgent need for more treatments, the MoH raised the maximum to accommodate Gilead's offer.

The fourth tender (161/2021) was designed for a small purchase of sofosbuvir alone. Despite this tender being for only 5% of the purchase volume of the first tender, the MoH set the same maximum price, to which Blanver had only agreed as a one-off offer. Blanver was the only seller placing an offer, but it was above the maximum, so there was no purchase.

Under the directive of focusing on pangenotypic treatments, the fifth tender (28/2022) involved sofosbuvir+daclatasvir, velpatasvir/sofosbuvir, or glecaprevir/pibrentasvir. Despite Blanver and Gilead placing offers, there was no effective competition because Blanver was disqualified since no offer was made for daclatasvir, and both drugs had to be bought together. Blanver was also disqualified on technical grounds because it listed the price per tablet, not treatment. Meanwhile, Gilead offered velpatasvir/sofosbuvir at the same price as the third tender after the exchange, which meant a real-term 7% discount in dollars. Still, this was above the maximum price for the tender, which Gilead claimed had been estimated based on another regimen, but the MoH denied it. Gilead also tried to add a disqualification for Blanver based on patent exclusivity, indicating that it had a granted patent. Again, the auctioneer rejected this appeal based on an understanding that Blanver could circumvent the patent. Lastly, Gilead argued that the tender should not have included daclatasvir and sofosbuvir since there was no version of daclatasvir on the market. The auctioneer replied that these drugs were included based on an expectation that a generic daclatasvir would be launched in time.[70]

[70] As shown in Section 4.2, the first generic daclatasvir was only approved in December 2022, after the tender.

Coming from two failed processes, the sixth tender (78/2022) also focused on pangenotypic drugs but excluded sofosbuvir+daclatasvir. The only two sellers were Gilead and Elfa, a distributor of Gilead's product. However, there was no competition since Elfa's price was much higher than Gilead's. Gilead's winning offer was 8% less in dollars than in the fourth tender, and it agreed to a further 2% discount as negotiated by the auctioneer.

Since then, the MoH has directly negotiated three contracts with the public laboratories involved in PDPs. In October 2023, the MoH signed a Technical Cooperation Agreement with Fiocruz for daclatasvir and sofosbuvir. In January 2024, it also bought the same quantity of sofosbuvir for the same price but from Furp. These purchases were a great deal for sofosbuvir, 35% cheaper than the previous lowest price, which was negotiated in the first tender. However, the price of daclatasvir was 46% higher than BMS's best offer in the second tender because the product was sold by Fiocruz but manufactured by Pharco in Egypt (see Section 4.2). As a result, the combined price of sofosbuvir+daclatasvir was 14% higher than ledipasvir/sofosbuvir and 2% higher than velpatasvir/sofosbuvir in the second tender, which are still the two cheapest treatments the MoH has ever negotiated.

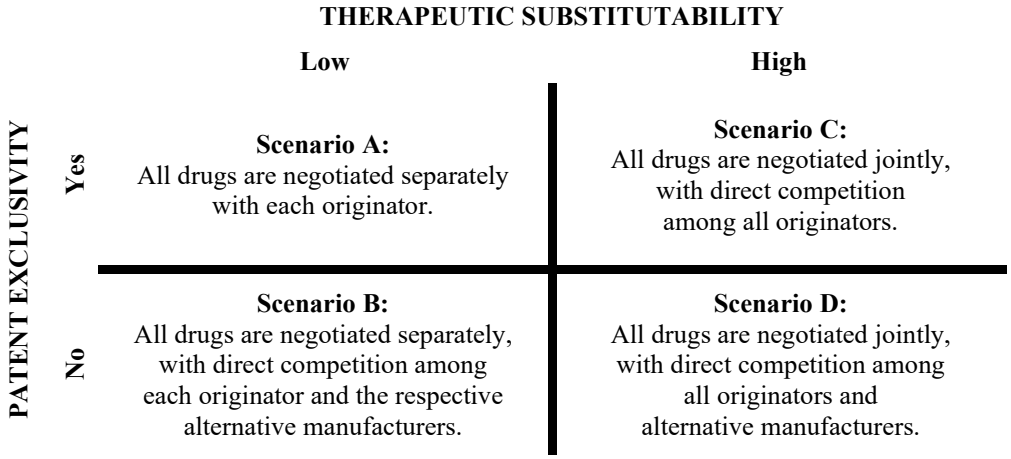
There are valuable lessons in this procurement history about how the government can effectively increase its bargaining power and reduce prices. It is not surprising that, once it became clear that sofosbuvir was not under effective patent exclusivity, the competition in the first tender between the originator and distributors of the generic version led to a significant discount. What sets this history apart is that, since the drugs are highly substitutable, the MoH could induce the most intense competition process in the second tender by having all originators and generic manufacturers compete. In that case, as demonstrated by Gilead, winning based on prices was more important than alleging patent exclusivity. The competition in the tenders might also have motivated discounts in subsequent direct negotiations.

Notwithstanding the potential benefits, this history also illustrates some limitations. The focus on pangenotypic regimens as recommended by the MoH left only three alternative treatments (see Section 4.1). However, two of these regimens are only sold by Gilead, and the sofosbuvir+daclatasvir regimen was not a suitable option for a while because there was no approved version on the market. As a result, the last four tenders were essentially direct negotiations with single sellers. Thus, this strategy depends on the existence of equally effective regimens from different manufacturers which are motivated to compete.

4.6 The strategy of induced competition

To discuss the findings presented so far, Figure 4.2 shows a matrix of four scenarios of patent exclusivity and therapeutic substitutability. In scenario A, all drugs are under exclusivity and differ significantly in effectiveness, so each contract must be negotiated individually with originators. In scenario B, different drugs are still regarded as therapeutically distinct, but the lack of patent exclusivity for a given drug means that there are multiple versions available, so the government may place the originator and generic manufacturers in direct competition – though still separately from other drugs. In scenario C, all drugs are patented and highly comparable in effectiveness, so the government may induce direct competition, but solely among originators. In scenario D, effectiveness is highly comparable and at least one drug is not under exclusivity, allowing the government to induce direct competition among originators and generic manufacturers.

Figure 4.2. Scenarios of competition based on patent exclusivity and therapeutic substitutability



To compare the scenarios, lessons are drawn from the empirical literature. Drug prices tend to be less affected by competition between drugs under patent exclusivity if substitutability is low or there are few alternatives (Barrenho et al. 2023). Meanwhile, generics tend to be considerably cheaper than originator products, although prices vary considerably depending on the country (Wouters et al. 2017; CGD 2019). Souza et al. (2023) found that most generics were at least 60% cheaper than the respective originator products in Brazil. However, the price of originator products may increase rather than go down after generic entry if the originator's market share is not challenged in what is called the generics paradox (Regan 2008). Thus, scenario D should have the highest competition level and scenario A the lowest, but future empirical studies with more data should investigate how scenarios B and C rank in the middle.

Applying these concepts to the history of HCV drug procurement in Brazil, all direct purchases were cases of scenario A. The first tender included the originator and distributors of the generic sofosbuvir, so it was scenario B. The second tender included all drugs, with multiple originators and one generic manufacturer, representing scenario D. All other tenders were instances of scenario A since the government effectively negotiated with only one seller. The third and sixth could have been scenario C because they included different regimens under exclusivity. The fourth could have been scenario B since it was again restricted to sofosbuvir. The fifth could have been scenario D because it involved drugs with and without exclusivity.

The most significant discounts in the sample happened in the first (scenario B) and second tenders (scenario D). The biggest discount happened in the first, but the originator did not try to compete, perhaps because it assumed patent exclusivity would justify disqualifying the generic or because the government asked for too big a discount. In the second tender, the pressure of competing with a generic manufacturer and other originators led to multiple sellers giving considerable discounts. Considering prices in Reais, the MoH has yet to negotiate cheaper treatments than at this tender, even considering direct negotiations with public laboratories in PDPs.

Comparing prices of HCV drugs in 65 countries between 2013 and 2019, Hudzik et al. (2023) found that Brazil had the second biggest price reduction as a percentage of GDP per capita (48%), only behind France (50%). The lowest prices in United States Dollars negotiated by the government were $1,331 for sofosbuvir+daclatasvir in October 2023 and $1,352 for velpatasvir/sofosbuvir in March 2019. A report from the Clinton Health Access Initiative argued that Brazil managed to reduce HCV drug prices ‘as a result of a national competitive tender with significant volumes and commitment’ and the protection of only secondary aspects of sofosbuvir, ‘which allowed for generic production through public-private partnerships despite ongoing legal challenges related to Intellectual Property’ (CHAI 2023 p.35). However, the Brazilian prices are still much higher than the generic alternatives produced in other low- and middle-income countries: sofosbuvir+daclatasvir costs $48 in Egypt and $39 in India, while velpatasvir/sofosbuvir costs $165 and $105, respectively (CHAI 2023).

Based on these findings, one may argue that the government induces competition in scenarios C and D. If a drug is under patent exclusivity, there is only one supplier, so it is reasonable to consider direct negotiation as the only procurement route. However, the drugs being highly comparable in effectiveness makes the government differentiate them less,

especially after focusing on pangenotypic drugs. Having at least one drug in the public domain, as in scenario D but not in C, increases the substitutability and strengthens this strategy. Therefore, the inventiveness lies in recognising that therapeutic substitutability allows the government to see all regimens, under exclusivity or not, as equally good substitutes, so it may simply buy the cheapest and maximise the purchase volume. This places the government in a much better position, especially when at least one drug is not under exclusivity. However, the government should never ignore significant differences in effectiveness to artificially produce the necessary conditions for this strategy. Effectiveness should remain a technical assessment to ensure access to quality treatment.

This strategy is different from mere generic competition as in scenario B. There is nothing new about countries and international institutions using tenders to reduce drug prices via generic competition (Maniadakis et al. 2018; Parmaksiz et al. 2022). The novel strategy is focused on competition among patented drugs, which other countries have only recently started exploring (Wouters et al. 2019; Barrenho et al. 2023). Like in Brazil, these tenders under exclusivity have led to considerable price reductions and were most often organised by the therapeutic class or indication.[71] Even the industry has highlighted the benefits of tendering with and without exclusivity (Roediger et al. 2019).

Nevertheless, scholars and the industry have also pointed to the risk of pharmaceutical tendering leading to market concentration (Wouters et al. 2017; Maniadakis et al. 2018; Roediger et al. 2019; Parmaksiz et al. 2022; Barrenho et al. 2023). By aggressively reducing drug prices, pharmaceutical tendering may render some market segments less attractive to companies, especially under patent exclusivity. Indeed, AbbVie, BMS and MSD did not participate in any tender after the aggressive competition in the second. Three common suggestions to prevent these effects are segmenting the tender to avoid a single-award system leading to a complete failure, combining price analysis with the overall economic cost of the supply to have a broader approach to the award criteria, and monitoring the supply to evaluate the success of procurement processes beyond the signature of a purchase contract.

One may argue that inducing competition between patented drugs with high substitutability is an *ex-post* intervention by the government that effectively curbs the patent

[71] Tendering has also been used for vaccines. However, these are harder to place in the matrix since exclusivity might come from factors other than patents and since the level of differentiation of biological products tends to be greater. A good example is the COVID-19 Vaccines Global Access (Covax) initiative (Parmaksiz et al. 2022).

exclusivity. While this strategy does lead to buyers having more clarity about purchasing options and the private returns of patents being potentially reduced, it does not allow third parties to exploit the patented drugs, so there is no *ex-post* change to patent exclusivity. What would constitute an *ex-post* intervention is, for example, the declaration of compulsory licences to incentivise local production during health emergencies like a pandemic.[72] That was not the case for any drug studied in this chapter. Therefore, the strategy here outlined builds on the patent exclusivity and therapeutic substitutability as they are and only produces an alternative procurement strategy that strengthens the bargaining power.

This case study also shows that the prospect of selling to the government is a relevant driver for manufacturers to seek, maintain and protect exclusivity over their inventions. Section 4.4 showed that originators discontinued drugs and even let granted patents lapse after the government removed the drugs from treatment guidelines (elbasvir/grazoprevir, simeprevir, 3D) or when the originator lost interest in competing in this market (daclatasvir). Via the same mechanism, Gilead has been fighting considerably hard for exclusivity over sofosbuvir at the INPI, despite facing the most intense opposition, and in tenders, despite the government refusing to accept exclusivity based on secondary aspects or pending applications. Therefore, other public policies like the definition of treatment guidelines and procurement strategies can affect applicants' behaviour towards their patent applications. However, that again does not constitute an *ex-post* corrective measure per se, but rather a reflection of the complex nature of patents as a strategic method of appropriation of pharmaceutical inventions.

These findings are in line with other policies that the government may employ to increase its bargaining power and influence prices. Investigating HCV drug procurement before 2015, Chaves et al. (2017) concluded that centralised direct negotiations were instrumental in lowering prices and expanding access. Section 4.5 showed how these negotiations led to consecutive discounts but at lower levels than the tenders.

Many studies stress the importance of PDPs in promoting local productive capabilities, especially since all generic versions of HCV drugs were involved in PDPs (Achcar and Fonseca 2024; Fernandes et al. 2024). However, more than the PDPs, what determined that generics were only registered for daclatasvir and sofosbuvir was that the combination regimen was

[72] Specialists interviewed for this thesis argued that compulsory licensing could affect the originators' willingness to join PDPs. On the one hand, they might join to avoid a compulsory license. On the other hand, they might fear the risk of capacitating a possible competitor if the government decides to issue a compulsory license.

recommended for HCV treatment and was not under effective patent exclusivity (see Section 4.4). The PDPs were established under considerable uncertainty around patent exclusivity, leading the MoH to suspend the sofosbuvir PDPs from 2018 to 2023 despite buying the generic from Blanver at the same time. In addition, the MoH is not obligated to honour the promise to procure drugs from the licensor, which considerably impacts the PDP's credibility. Future studies should investigate if the government was right to use PDPs for these drugs to develop capabilities in public laboratories or if it should have simply invested in supporting the local production by private firms like Blanver and EMS.

Finally, another policy believed to make drugs cheaper in Brazil is the price regulation by Anvisa, which sets price caps for sales to final consumers and the government (Salomão and Ido 2021). Yet, this policy had no relevance to centralised procurement. Given the large purchase volumes, the maximum prices established by the MoH for each tender were much lower than Anvisa's caps. The prices were, on average, 90% cheaper than the caps, with the biggest difference being the purchase of ledipasvir/sofosbuvir in the second tender for 97% less than the cap. A similar argument was used by the Administrative Council for Economic Defence (CADE) when refusing to proceed with a representation against Gilead for allegedly abusing its economic powers by raising the price of Sovaldi after the first sofosbuvir grant. Based on preliminary proceedings, CADE concluded that raising prices in small purchases while still below Anvisa's caps is not anti-competitive, especially given the constant price reductions in centralised procurement (CADE 2022). Therefore, although possibly relevant for smaller purchases, Anvisa's price caps are too high to affect centralised procurement. Some also argued that, by not being revised and only being adjusted every year to reflect inflation and industry-wide productivity changes, they become misaligned with market trends (Miziara and Coutinho 2015; Souza et al. 2022).

4.7 Conclusion

This chapter investigated the Brazilian MoH's strategy of inducing competition in the centralised procurement of HCV drugs by having originators of substitute treatments compete among themselves and with generic manufacturers. This strategy significantly boosted the government's bargaining power and reduced drug prices, which is essential for the goal of eliminating HCV as a public health threat by 2030.

This study involved a mix of data analyses: reading the treatment guidelines, identifying the products approved for marketing, mapping the patent landscape, and investigating the procurement history. It identified the two key factors that led to this strategy having positive effects: a) having restricted treatment to alternative regimens that were virtually equal in effectiveness, the MoH could shift from cost-effectiveness analyses to simply buying the cheapest alternative; and b) the existence of robust patent opposition mechanisms and a nuanced approach to patent protection allowed for the launch of generic alternatives. As a result, the government induced competition among originators and generic manufacturers, reaping the benefits of the PDPs despite originators' claims of exclusivity based on pending applications and non-constraining patents.

Still, this strategy is hindered by market concentration, either because there are fewer competitors or because they refuse to join the tenders. Thus, the government should invest in developing local productive capabilities and making tenders more attractive for originators and generic manufacturers. These efforts should be helped by the introduction of two pangenotypic regimens: sofosbuvir/velpatasvir/voxilaprevir and sofosbuvir+ravidasvir. The former was registered by Gilead under the name Vosevi and approved for incorporation into SUS but has not yet been included in the guidelines or purchased (MoH 2022b). The latter is an unpatented technology developed by the Drugs for Neglected Diseases Initiative (DNDi) in response to the opposition to the patenting of sofosbuvir and the selective licensing from Gilead (Douglass et al. 2018), which Pharco is transferring to Blanver and Fiocruz (Fiocruz 2023; DNDi 2024).

Based on these findings, a matrix of four scenarios was developed considering the level of patent exclusivity and therapeutic substitutability to understand how the different actors interact. Since there were few purchases to analyse and they did not represent all scenarios, this chapter could not statistically determine the impact on bargaining power. Still, the results are in line with the literature on competition in public procurement and drug prices. They also show that, while public health policies like the definition of treatment guidelines and procurements strategies may affect applicants' interest in pursuing patent protection, these should not be seen as *ex-post* corrective patenting policies. Instead, this relationship results from the complex use of patents as an appropriation strategy for pharmaceutical inventions.

This chapter also discussed how other policies affected this strategy. While helpful, the PDP programme was not the determinant of generic competition, and there are significant issues with the programme and its incentives. Although Anvisa's price regulation is believed

to have a strong influence over the pharmaceutical market, it played no meaningful role in centralised procurement because the caps were much higher than the negotiated prices.

Future studies should analyse other diseases and contexts to include all competition scenarios. They should investigate the strategy of inducing competition in contexts without incentives, like the PDPs, or with smaller purchases, where price controls might be relevant.

Finally, this study has corroborated the findings of Chapter 3 about Anvisa submitting non-binding opposition which contributed to a high level of scrutiny for pharmaceutical patent examination, thus increasing the positive effects of the strategy of inducing competition. However, this study also echoed the conclusion of Chapter 2 about the Backlog Reduction Plan leading the INPI to grant more often. With the Plan, and now that the dual examination system has been abolished, more drugs might be patented, and this protection might be longer and broader. Therefore, Brazil should evaluate its patent policies to ensure it preserves the legacy of rigorous examination developed with the help of Anvisa while also promoting the efficiency that is necessary to ensure balanced stimuli in the patent system.

5 CONCLUSION

The work for this thesis started in September 2019, before the COVID-19 pandemic forced the entire world to discuss pharmaceutical IPR policies. In the academic bubble, proposals of flexibilities in patent policy to address developmental and public health challenges have been made for decades as a countermeasure to the strengthening of IPR protection after TRIPS and subsequent free-trade agreements (Correa 2000; 2014; 2022; Deere 2009; t' Hoen et al. 2018; Shadlen 2017; Shadlen et al. 2020; Tenni et al. 2022). When suddenly the world needed therapeutics by the hundreds of millions and vaccine doses by the billions, the cracks in the current state of affairs in the pharmaceutical industry became more evident, and fixing them became more urgent.

This thesis analysed how the patent system can be perfected while preserving its core institutions such as the TRIPS Agreement. However, one should not read into this a subscription to the system. Instead, this is a pragmatic approach that stems from a recognition that the system, in the least, does not work as well for everyone, and that there are immediate changes that can and should be implemented so that it produces more equitable results.

Lessons were drawn from the history of pharmaceutical patenting in Brazil because the country has proactively exercised creativity in policy design, introducing measures to promote speed and rigour in patent examination. This investigation is based on the recommendation that developing countries should invest in strengthening patent examination as a preventive (*ex ante*) measure to promote the balance stimuli of patents instead of relying on corrective (*ex post*) measures to correct errors that result from lax examination.

This chapter is divided into three parts. First, the main contributions to patent policy and the empirical literature, considering the three case studies. Second, a discussion of the limitations of this thesis and suggestions for future research. Third, the concluding remarks.

5.1 Contributions

The main goal of this thesis was to contribute to the design of better policies, making the patent system more effective in producing the balanced stimuli expected from patents. Nonetheless, the analyses provide insightful contributions to the empirical literature regarding possible case studies, data sources and selection, and analytical methods. This section discusses this policy and academic contributions.

5.1.1 Patent policy

The findings of this thesis show that the dual examination system led to a convergence of Anvisa and the INPI at high examination standards, with higher scrutiny of all patentability criteria, not just the traditional requirements of novelty, inventiveness and industrial applicability. The higher relevance given to invention description is consistent with the goal of producing balanced stimuli with patents by guaranteeing the necessary level of knowledge disclosure to compensate for the temporary exclusivity. After much conflict and uncertainty, this system became mutually beneficial and almost symbiotic once the entities agreed that Anvisa contributed the most when focusing on applications related to strategic products for SUS and submitting non-binding oppositions when issues were found, which the INPI then considered in its own examination. Ironically, when this policy finally started working well, it was abolished.

As a first recommendation from this thesis, Anvisa must continue submitting non-binding oppositions as any third party can do. It currently depends on the MoH, which should proactively use this mechanism to assist in the examination of strategic applications for SUS. In a more complex effort, the task of examining strategic applications to evaluate when non-binding oppositions may be submitted should be solidified in Anvisa's governing law as one of its key roles to preserve this important contribution to the Brazilian patent system. Similarly, other countries should explore the involvement of health regulators via non-binding oppositions. Moreover, similar policies could also be introduced for other strategic sectors where patents are a more common and effective appropriation strategy, e.g. telecommunications, animal health and agriculture.

The dual examination system was abolished shortly after the INPI introduced the Backlog Reduction Plan. These decisions are part of a commitment to making decisions as fast as possible to reduce the backlog, but they also show a preference for influence from developed countries' patent offices instead of Brazil's own health regulator. If the INPI was looking for reports on which to base the examination and expedite prosecution in Brazil, why were Anvisa's contributions discarded? They had, after all, been written specifically for the applications filed at the INPI, examined based on the LPI and went beyond the prior art search report. They should have been more adequate and effective than the imported reports in substituting for the work by the INPI examiners.

Considering that the end goal is backlog reduction, it can be argued that the INPI was more successful when it hired more examiners in 2017. Apart from an initial wave of abandonments after the Plan was introduced, the rate of backlog reduction has been slowing down, and Brazil still has 115,414 pending applications as of February 2024, which amounts to 365 per examiner. Contrary to expectations, the Plan has made examinations take much longer than before, which suggests that forcing examiners to base their analyses on someone else's work deprives them of an important step in obtaining the knowledge necessary to examine applications, leading to slower decisions. While the Plan has reduced the overall prosecution lag, this is mostly achieved by the examination starting earlier, and the effects on grant rate have been more significant than on the duration of processes. The results show that examiners are much more likely to grant patents, even when compared with 14 other offices to control for characteristics of the inventions, and much less likely to make objections before granting. These results suggest that the Plan might be reducing examination rigour in Brazil.

In that sense, another recommendation of this thesis is to end the Backlog Plan and invest in other measures that strengthen examination and more effectively deal with the administrative imbalance between examiners and the backlog. Most importantly, the INPI has too few examiners for the volume of pending applications. It is a good sign that the office hired new examiners in 2024, but it might still be understaffed. Moreover, the office could invest in tools that assist the examination, like more powerful search engines, while also considering the biases that might influence these tools to avoid compromising rigour.

The history of centralised procurement of HCV drugs by the Brazilian government shows that the preventive measures implemented to strengthen patent examination, most importantly Anvisa's non-binding oppositions, were instrumental to guaranteeing that protection was only given when warranted. This approach to patent exclusivity, in a context where multiple alternative treatments were considered great substitutes for similar cases, allowed the government to explore a novel procurement method: induce competition in tenders by including originators and generic manufacturers of different drugs, all competing on the lowest price per treatment. This has significantly increased the government's bargaining power and allowed for bigger discounts.

Another recommendation based on these results is that the comparison of therapeutic effectiveness between alternative treatments remain technical to ensure access to quality treatment, instead of being declared to reproduce the conditions for inducing competition.

Therefore, this strategy is contingent on the availability of equally effective alternative treatments. What the government can do is boost the effects of the strategy by investing in local production capacity to explore the opportunities for competition opened by strong patent examination policies and a nuanced approach to patent exclusivity, which together ensure protection is only given when warranted. In special circumstances like a pandemic, the government may even apply *ex-post* measures to temporarily curb patent exclusivity by issuing compulsory licenses, for example. However, the removal of Anvisa from examination and the introduction of the Plan have led to more frequent grants, which may reduce such opportunities for generic competition. Still, the strategy of induced competition could boost bargaining power among originator products only, so it is a powerful policy tool that any government in the Global South or North may implement to address the public health challenges.

In summary, the three case studies show that there is considerable leeway for governments to implement patent policies that are TRIPS-compliant while still addressing pressing developmental and public health challenges. The dual examination system in a reduced form, where the health regulator submits non-binding oppositions to strategic applications, is an effective way to promote patent examination rigour. On the contrary, importing prior art search reports from other offices was more effective in increasing the rate of grants and grants without any examiner objection than expediting examination and overall prosecution. The history of HCV drug procurement illustrates why the literature recommends that developing countries invest in preventive measures like the dual examination system instead of simplifying examination, as under the Plan. While Anvisa's opposition contributed significantly to a high standard of patenting that allowed for generic competition to boost the benefits of the strategy of inducing competition in tenders, the Plan has led other drugs to obtain patents much more frequently, which restricts the opportunities for generic competition and reduces the government's bargaining power in centralised procurement. Therefore, this thesis shows that *ex-ante* pharmaceutical patent examination policies significantly affect the pharmaceutical market and strengthen other public policies, especially in developing countries.

5.1.2 Empirical analyses of patent prosecution and outcomes

The empirical literature on patents rarely travels South of the political equator. Few large-sample studies have used data from developing countries to investigate patent prosecution policies (Tong et al. 2018; Abinader 2020; de Rassenfosse et al. 2021; Zhu et al.

2022; Yang et al. 2024). Chapter 2 is the first large-sample analysis of Brazilian pharmaceutical patenting data. Previous studies of the country focused on smaller samples (Silva 2008; Sampat and Shadlen 2015; 2017; Mercadante and Paranhos 2022).

Furthermore, there have been calls for the implementation of TRIPS flexibilities especially by developing countries for the past three decades since TRIPS was signed (Musungu and Oh 2006; Deere 2009; Correa 2014; 2022; Oswald and Burri 2021). However, there are few empirical analyses, which also tend to have smaller sample sizes (Sampat and Shadlen 2015; 2017; 2018; t' Hoen et al. 2018; Sarnoff 2020; Tenni et al. 2022). Therefore, this thesis provides an insightful and novel analysis that should help inform this debate.

What is especially interesting is that the data used for this study was extracted from the EPO's PATSTAT database, which is one of the most common patent data sources because it includes bibliographic and legal event data from dozens of offices around the world (Martínez 2011; Schwartz and Sichelman 2018; EPO 2024a; 2024b; 2024c). The international comparison of grant rates provided in Chapter 2, between the INPI and 14 patent offices from countries equally divided between the Global North and South, demonstrates that quality data is available for studying developing countries. If the patent system does not work the same way for everyone, the literature should look beyond the few countries that seem to benefit the most.

In terms of the methodological choices that allowed for the case studies, this thesis explores different methods for selecting pharmaceutical applications which go from the broadest to the most specific, mirroring the empirical strategies of the chapters.

In Chapter 2, the goal was to investigate the history of pharmaceutical patent examination, covering as many applications as possible. Thus, pharmaceuticals were defined technically based on IPC codes, with data being extracted from PATSTAT (EPO 2024a).

In Chapter 3, the scope was reduced to focus on the pharmaceutical applications that needed Anvisa's consent before being granted by the INPI. One simple selection method would be to look at applications with a decision from Anvisa. However, as discussed in Subsection 3.2.2, the order of examination was flipped in 2013. From that year, all applications that needed Anvisa's consent went there first. Before 2013, the INPI was the first to examine applications and only forwarded to Anvisa the applications it intended to grant. Throughout the two decades of the mechanism, there were disagreements between the two entities on the parameters that determined if an application needed consent. Therefore, there is no way to know for sure which

applications rejected by the INPI would have been sent to Anvisa had the INPI's first decision been positive. One way to replicate this *sui generis* selection process, although not perfect, is to use the same IPC classification as described in Chapter 2. Finally, the goal was to compare the grounds for negative decisions, which required access to the decision documents. Thus, Chapter 3 used a mix of selection methods, combining data from PATSTAT, Anvisa's prior consent records, and the INPI's Buscaweb database (Anvisa 2022b; EPO 2024a; INPI 2024f).

In Chapter 4, the analysis was even more focused, covering just the patent applications that covered the drugs and combinations recommended for HCV treatment in Brazil since 2015. Given the challenges of landscaping patent applications from scratch since many applications can cover one drug and each application can also cover many other drugs, this chapter employed multiple selection methods to define the relevant patent families. First, it searched international databases that link patent applications and drugs such as the Orange Book and MedsPaL (FDA 2023; MPP 2023). Then, it drew on patent landscaping reports on HCV drugs that have been published by international institutions (WHO 2016; UNITAID 2015a; 2015b; 2017a; 2017b; 2017c) and the MoH's requests for fast-tracking of strategic applications (INPI 2019f). Based on the families identified in these sources, the chapter searched for Brazilian twins and divisionals in the Buscaweb database (INPI 2024f).

Finally, the different selection methods applied have implications for the analytical methods. The most automated and single-source approach applied in Chapter 2 allows for a large-sample quantitative analysis. The analysis in Chapter 3 is restricted by the need to search for applications on the Buscaweb database manually, the availability of documents, and the need to read the decisions to identify which articles were cited as grounds for rejections, creating the data for the analysis of citation rate. Lastly, the mixed-methods analysis in Chapter 4 combines multiple sources and is built by consulting treatment guidelines and drug registration records, searching for applications manually and reading the different documents to understand the prosecution histories, and analysing the procurement history in government databases and records from negations in tenders.

5.2 Limitations and future research

The main limitation of this thesis is that it only analyses preventive (*ex ante*) policies implemented by Brazil to strengthen pharmaceutical patent examination. Since there is no

analysis of corrective (*ex post*) measures, the thesis cannot test if preventive measures are indeed more effective, as suggested in the literature. Therefore, future studies should investigate, for example, the post-grant opposition and legal challenges based on imported reports under the Backlog Reduction Plan, comparing them with grants that happened outside of the Plan. If opposition and challenges have become more frequent and likely to succeed, it would support the understanding that the Plan has reduced examination rigour in Brazil.

The dimension of patent quality is another limitation of the thesis. While the findings in Chapter 2 and Chapter 3 point to a reduction in pharmaceutical patent examination rigour in Brazil, the research cannot establish a causality with patent quality. Future studies should investigate the quality of patents granted under or outside the Plan and with a negative or a positive first decision from Anvisa to evaluate if the apparent effect on rigour had significant consequences for patent quality. For example, studies could investigate the scope of the claims or the backwards and forward citations between applications.

Ideally, the analysis in Chapter 2 would control for applications under fast-tracking since this is an indicator of invention importance that many have suggested significantly affects the likelihood of grant and the duration of prosecution (Harhoff and Wagner 2009; Yamauchi and Nagaoka 2015; Yang et al. 2024). Unfortunately, the INPI stopped reporting to PATSTAT when applications were fast-tracked in 2019 (INPI 2019e; EPO 2024b). Future studies should include control for this when analysing the outcomes and duration of prosecution.

Something that is hinted at but not analysed in Chapter 2 is the applicant's interest in some delay in prosecution (Harhoff and Wagner 2009; Mercadante et al. 2018; Zhu et al. 2022). Future studies should measure how much and why applicants might be wilfully delaying prosecution in Brazil. This is important information because it introduces a basic question to the assumption that the patent office should try to decide as fast as possible.

The analysis in Chapter 3 is restricted to the grounds for rejections cited in final negative decisions. Thus, it cannot capture whether or not the INPI or Anvisa noticed other issues in their preliminary reports that were sufficiently dealt with by the applicant and were not cited in the final decision. By not looking at the original application and positive decisions, the chapter also cannot determine how much the text changed from applications as requested by the examiners. Future studies should devise strategies that allow for large sample analyses while also including all the necessary documents from the prosecution of each application.

Especially in Chapter 3, it would have been interesting to have data on the type of invention covered by the applications, since it has been suggested that, if not by design, Anvisa's contribution to examination naturally developed as an increase in the scrutiny of secondary applications (Shadlen 2011; 2017; Guimarães and Corrêa 2012; Correa 2014; Sampat and Shadlen 2015; 2017). If that is the case, one should expect the INPI and Anvisa to have disagreed more frequently on secondary than primary patents. If, however, Anvisa simply had a baseline standard for granting patents that was higher than the INPI's, one might expect disagreements to happen more often for primary than for secondary applications. Future studies should evaluate when the entities disagreed more often and investigate if the explanations proposed adequately explain the differences.

In Chapter 4, a matrix of four scenarios was proposed to represent how patent exclusivity and therapeutic substitutability affect competition in the centralised procurement of drugs. However, the case study of centralised tenders for HCV drugs does not include all scenarios because, in many cases, the tenders effectively had only one seller. By only looking at centralised procurement by the MoH, purchase volumes were so high that the negotiated prices were significantly lower than Anvisa's price caps. Future studies should compare the results with other drugs where all four scenarios indeed happened, including smaller purchases on which Anvisa caps are more likely to have an effect.

Lastly, notwithstanding the international comparison of grant rates in Chapter 2, all three chapters were essentially single-case studies. Future studies should conduct similar analyses in other developing countries to draw other lessons about the use of TRIPS flexibilities. There is a scholarship on Argentina's 2012 examination guidelines and India's Section 3(d) but with smaller samples and covering less than a decade after both countries implemented pharmaceutical patenting (Correa 2014; Oswald and Burri 2021; Sampat and Shadlen 2015; 2017; 2018). Now that time has passed, one can evaluate the effect on outcomes of large samples of applications prosecuted by Argentina, Brazil and India to analyse how these measures influenced the criteria cited as grounds for negative decisions, as in Chapter 3.

5.3 Concluding remarks

The history of pharmaceutical patent policy in Brazil is rich with examples of how this country has always been a trailblazer. In the 19th century, it was a trailblazer for the entire

world. In 1804, it became only the fourth country to introduce specific legislation for patents and implemented early on most of the changes that would motivate the first international treaty on IPRs, the 1883 Paris Convention.

During the 20th century, Brazil was again at the forefront of the patent policy discussion domestically and internationally under the heavy influence of political and economic ideologies. Throughout most of the century, it was committed to a developmental agenda, banning patenting for pharmaceutical products in 1945 and processes in 1969 and leading the international fight against restricting nations' capacity to use IPR policy for development as the then already-developed countries had done in the past. Towards the end of the century, a shift in government to neoliberal ideologies combined with intense lobbying from IPR-intensive sectors and explicit pressure from the United States via trade sanctions led Brazil to sign the 1994 TRIPS Agreement and go beyond the mandatory minimum reform. Examples of TRIPS-plus dispositions implemented were the introduction of pharmaceutical patenting in 1997 instead of the 2005 deadline, the pipeline system, and the patent term extension clause.

In the first quarter of the 21st century, Brazil has repeated a version of the previous century. On the one hand, it has returned to a more developmental approach, implementing strong TRIPS flexibilities like the dual examination system with Anvisa and abolishing the term extension clause. On the other hand, it has also implemented policies like the Backlog Reduction Plan and did not support the TRIPS waiver during the COVID pandemic.

This thesis focuses on the dichotomy of policies implemented in the 21st century, investigating the Plan's effects on examination speed and grant rates, Anvisa's contributions to pharmaceutical patent examination rigour and the consequences for competition in centralised tenders for drug procurement. These policies and their effects are analysed based on the recommendation that developing countries should strengthen pharmaceutical patent examination as a preventive (*ex ante*) measure to promote a balance between the private and public incentives in the patent system.

The three case studies exemplify how patent examination policies have repercussions outside the patent office. The dual examination by Anvisa and the INPI raised the patent examination rigour and promoted opportunity for generic competition, which boosted the government's bargaining power in centralised tenders for equally effective alternative HCV treatments. However, the Backlog Reduction Plan decreased scrutiny at the INPI, making it grant patents more often and make fewer objections. The effect on the HCV drug market has

been that the INPI granted patents a lot more often once the dual examination system was removed and the Plan was introduced, which could limit future generic competition and the government's bargaining power in the strategy of inducing competition.

Other countries should see in the case studies evidence that they can and should implement TRIPS flexibilities and that strengthening pharmaceutical patent examination is a strategy that has positive results for public health policies. This should be a lesson to all, especially countries in the Global South. For Brazil, this thesis shows that, while the INPI has developed a high patenting standard, recent policies that have simplified examination to expedite prosecution threaten this standard, creating a prospect of lax examination that may lead to lower patent quality. The next years will show if Brazil remains a trailblazing leader of the Global South or has become a follower of the leaders of the Global North.

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Appendix A: dual examination of pharmaceutical patent applications in Brazil

Between 2001 and 2021, there were two important changes in how Anvisa interacted with applicants: the communication channel and if applicants had a say before Anvisa's final decision. Initially, the INPI often refused to forward Anvisa's decisions to applicants. In 2008, Anvisa started publishing reports in the Union's Official Gazette, which it did until the mechanism was abolished. In addition, Anvisa published preliminary reports before the final decision, and applicants could reply to these reports with counterarguments or amendments to the applications. After the 2017 Joint Ordinance was passed, it only issued preliminary reports before the final decisions if there were references to banned substances. When the issues were restricted to the other criteria, it published the final decision without interacting with applicants since this was a non-binding PGO. Thus, Anvisa expedited the process by submitting its original opinion to the INPI.

In addition, the lack of definition about which pharmaceutical product and process patents required prior consent sparked unavoidable disagreements. While not all pharmaceuticals required it (e.g., cosmetics), some non-pharmaceuticals did (e.g., agrochemical inventions that referenced use in humans). Since there was no clear technological cut, the INPI had to read each application to decide when to send it to Anvisa. For its part, Anvisa would reassess the applications, sometimes returning them to the INPI because it thought they did not need its consent. More than an error, these returned applications reveal conflicts around what inventions needed consent. Another evidence of the complexity of this *sui generis* selection process is that it took almost two decades of learning by doing for the entities to publish manuals, which were clearer about the inventions that did not need consent than those that did (INPI 2018c; Anvisa 2020).

From 2013 to 2021, Anvisa had to check whether the invention was related to strategic products for SUS to determine which articles of the LPI would be considered. Summarising this highly complex process, applications were selected in two stages (Anvisa 2020).

First, examiners searched the Cortellis database for pharmaceutical products directly or indirectly referenced in the claims, their development stage, and if they had a therapeutic indication in one of the strategic classes. The product was considered strategic if the therapeutic indication was listed in the MoH's Ordinance nº 736/2014 and the status was pre-registered, recommended approval, registered or launched. If no strategic product was found, the examiner searched for explicit references to products or compounds in the claims and used Cortellis to

find the corresponding active pharmaceutical ingredient and identify the therapeutic indication of the product with the most advanced development status. In this case, strategic products had to be in the MoH's list of indications and the status had to be launched or registered.

Then, examiners checked if the product was in the several strategic lists for SUS. The lists were: a) the National List of Essential Medicines; b) the technological recommendations from CONITEC; c) the Clinical Protocols and Therapeutic Guidelines; d) the PDPs; and e) the patent applications under fast-tracking by the INPI as requested by the MoH.

As a result, there were three categories of applications: those whose therapeutic use Anvisa knew and considered relevant; those whose use Anvisa knew but thought not relevant; and those whose use Anvisa did not know. While Anvisa screened all applications for banned substances, it only considered the other articles of the LPI for the first category. The screening for banned substances was done by identifying the substances listed in the application either directly, when the specific substance was mentioned, or indirectly, when generic Markush structures could have included banned substances. To identify the substances, the examiner used the SciFinder database, which includes the lists of banned substances in Brazil according to the updated lists E and F of the MoH's Ordinance nº 344.

Appendix B: HCV patent landscaping in Brazil

The tables below contain 89 patent applications filed in Brazil covering the drugs in this study as of November 2024. Each table includes the applications covering the individual drugs or their combinations that are recommended by the MoH for HCV treatment. Therefore, this landscape should not be read as an exhaustive list of applications for any of the drugs. The tables include application numbers in Brazil, the priority filing and the WO number for PCT filings. Patentees are indicated alphabetically according to the names currently listed on the INPI's website, aggregated at the parent company level.

For each application, the tables include the date of filing, which is the international filing date for PCT applications, the outcome, and the outcome date. For granted patents, the tables indicate when they lapsed or are expected to expire. The prosecution was analysed to determine when applications were fast-tracked, if third parties submitted oppositions, if the applicant appealed any decision, if there was any litigation, and if the application was prosecuted under the Backlog Reduction Plan. Cases of fast-tracking were categorised according to three types: when the MoH requested it for applications related to strategic products for SUS; when applicants requested it after claiming that someone was exploiting the invention without their consent; or when applicants requested it as part of the special programme for strategic health technologies. Finally, nine types of Anvisa's involvement were categorised:

- *Abolished*: the dual examination mechanism was abolished before Anvisa's decision.
- *Consent opposed*: Anvisa gave consent based on banned substances but submitted a non-binding opposition or Anvisa denied consent before the 2017 agreement, after which the INPI considered Anvisa's denial as a non-binding opposition.
- *Forced consent*: the application was denied consent, but Anvisa was forced to give it by a court order.
- *Full consent*: the application was related to strategic products for SUS and had no patentability issue.
- *Interrupted*: the application was abandoned before Anvisa's decision.
- *Not involved*: the application was never sent to Anvisa because the INPI considered it was not relevant to human health.
- *Restricted consent*: the application was not related to strategic products for SUS and had no reference to banned substances.

Appendix B

Table B.1. Patent landscape for daclatasvir used for HCV treatment in Brazil

Application	Priority	WO	Harmonised patentee	Filing date	Outcome	Outcome date	Fast-tracking	Anvisa	Third-party opposition	Appeal	Litigation	Backlog Plan
PI0716220	US2007075545	2008/021928	BMS	09/08/2007	Abandoned	17/01/2017	MoH	Not involved	No	No	No	No
PI0716483	US200707554	2008/021927	BMS	09/08/2007	Granted but lapsed on 31/05/2022	09/10/2018	MoH	Consent opposed	Yes	No	No	No
PI0815142	US2008071734	2009/020828	BMS	31/07/2008	Granted but lapsed on 01/06/2021	25/09/2018	MoH	Consent opposed	No	No	No	No
PI0815611	US2008071696	2009/020825	BMS	31/07/2008	Granted but lapsed on 01/06/2021	21/08/2018	MoH	Full consent	No	No	No	No
BR112012008533	US2010051898	2011/046811	BMS	08/10/2010	Rejected	19/02/2019	MoH	Consent opposed	No	No	No	No
BR112012011134	US2010055045	2011/059850	BMS	02/11/2010	Abandoned	28/09/2021	-	Not involved	No	No	No	No
BR112012011100	US2010055565	2011/059887	BMS	05/11/2010	Abandoned	01/10/2019	-	Not involved	No	No	No	No
BR112012014729	CA2010001935	2011/072370	Boehringer Ingelheim	13/12/2010	Abandoned	17/01/2017	MoH	Not involved	No	No	No	No
BR112013002922	US2011046285	2012/018829	BMS	02/08/2011	Rejected	25/09/2018	MoH	Consent opposed	No	No	No	No
BR112014005617	US2012061085	2013/059638	AbbVie	19/10/2012	Removed	10/09/2019	-	Not involved	No	No	No	No
BR112014006314	US2012061075	2013/059630	AbbVie	19/10/2012	Abandoned	22/08/2017	-	Not involved	No	No	No	No
BR112014017266	US2013020954	2013/106520	BMS	10/01/2013	Abandoned	21/08/2018	MoH	Consent opposed	No	No	No	No

Table B.2. Patent landscape for dasabuvir used for HCV treatment in Brazil

Application	Priority	WO	Harmonised patentee	Filing date	Outcome	Outcome date	Fast-tracking	Anvisa	Third-party opposition	Appeal	Litigation	Backlog Plan
PI0816994	US2008076576	2009/039127	AbbVie	17/09/2008	Granted and valid	24/12/2019	-	Restricted consent	No	No	No	No
BR112012022774	US2011027511	2011/112558	AbbVie	08/03/2011	Abandoned	28/01/2020	-	Restricted consent	No	No	No	Yes
BR112012031500	US2011039769	2011/156578	AbbVie	09/06/2011	Abandoned	13/04/2021	-	Interrupted	No	No	No	No
BR112013001132	US2011044283	2012/009699	AbbVie	15/07/2011	Abandoned	10/03/2020	-	Consent opposed	No	No	No	Yes
BR112013001138	US2011044282	2012/009698	AbbVie	15/07/2011	Rejected	17/09/2019	-	Not involved	No	No	No	No
BR112015008927	US2013065760	2014/063101	AbbVie	18/10/2013	Abandoned	27/10/2020	-	Interrupted	No	No	No	No
BR112015033022	US2014045054	2015/002952	AbbVie	01/07/2014	Abandoned	04/05/2021	-	Interrupted	No	No	No	No

Appendix B

Table B.3. Patent landscape for elbasvir used for HCV treatment in Brazil

Application	Priority	WO	Harmonised patentee	Filing date	Outcome	Outcome date	Fast-tracking	Anvisa	Third-party opposition	Appeal	Litigation	Backlog Plan
PI1013394	US2010028653	2010/111483	MSD	25/03/2010	Granted and valid	19/04/2022	-	Abolished	No	No	No	Yes
BR112013007696	CN2011001638	2012/041014	MSD	28/09/2011	Abandoned	01/10/2019	-	Not involved	No	No	No	No
BR112013007725	US2011053562	2012/050850	MSD	28/09/2011	Removed	05/12/2017	-	Not involved	No	No	No	No

Table B.4. Patent landscape for glecaprevir used for HCV treatment in Brazil

Application	Priority	WO	Harmonised patentee	Filing date	Outcome	Outcome date	Fast-tracking	Anvisa	Third-party opposition	Appeal	Litigation	Backlog Plan
BR112013006693	US2011052304	2012/040167	Enanta	20/09/2011	Granted and valid	12/07/2022	-	Consent opposed	No	No	No	No
BR112015020918	US2014027556	2014/152635	AbbVie	14/03/2014	Abandoned	28/12/2021	-	Abolished	No	No	No	Yes
BR112015023017	US2014027423	2014/152514	AbbVie	14/03/2014	Granted and valid	30/08/2022	-	Abolished	No	No	No	Yes
BR112016022858	US2015023922	2015/153792	AbbVie	01/04/2015	Abandoned	03/11/2021	-	Restricted consent	No	No	No	Yes
BR112016022976	US2015023923	2015/153793	AbbVie	01/04/2015	Rejected	20/09/2022	-	Abolished	No	No	No	Yes
BR112016027366	US2015034371	2015/188045	AbbVie	05/06/2015	Granted and valid	16/07/2024	-	Restricted consent	No	No	No	Yes
BR112017028185	US2016039266	2016/210273	AbbVie	24/06/2016	Rejected pending appeal	31/10/2023	-	Abolished	No	Yes	No	Yes
BR112018000982	US2016042806	2017/015211	AbbVie	18/07/2016	Rejected	27/06/2023	-	Abolished	No	No	No	Yes
BR102018002956	US2015431906	-	AbbVie	15/02/2018	Abandoned	03/01/2023	-	Abolished	No	No	No	Yes

Table B.5. Patent landscape for grazoprevir used for HCV treatment in Brazil

Application	Priority	WO	Harmonised patentee	Filing date	Outcome	Outcome date	Fast-tracking	Anvisa	Third-party opposition	Appeal	Litigation	Backlog Plan
PI0718161	US2007022460	2008/057209	MSD	23/10/2007	Rejected	15/09/2020	-	Consent opposed	No	No	No	No
PI0916235	US2009050915	2010/011566	MSD	17/07/2009	Granted and valid	29/09/2020	-	Restricted consent	No	No	No	Yes
BR112013007725	US2011053562	2012/050850	MSD	28/09/2011	Removed	05/12/2017	-	Not involved	No	No	No	No
BR112014003798	US2012051177	2013/028470	MSD	16/08/2012	Abandoned	23/07/2019	-	Not involved	No	No	No	No
BR112014003802	US2012051168	2013/028465	MSD	16/08/2012	Abandoned	12/06/2018	-	Interrupted	No	No	No	No
BR112014010545	US2012062145	2013/066753	MSD	26/10/2012	Abandoned	16/05/2017	-	Not involved	No	No	No	No

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Table B.6. Patent landscape for ledipasvir used for HCV treatment in Brazil

Application	Priority	WO	Harmonised patentee	Filing date	Outcome	Outcome date	Fast-tracking	Anvisa	Third-party opposition	Appeal	Litigation	Backlog Plan
BR122014012810	US2010034600	2010/132601	Gilead	12/05/2010	Granted and valid	14/04/2020	-	Restricted consent	No	No	No	No
BR122014013631	US2010034600	2010/132601	Gilead	12/05/2010	Granted and valid	17/11/2020	-	Restricted consent	No	No	No	Yes
PI1010795	US2010034600	2010/132601	Gilead	12/05/2010	Granted and valid	11/12/2018	MoH	Consent opposed	No	No	No	No
BR112014006324	US2012055621	2013/040492	Gilead	14/09/2012	Granted and valid	26/12/2018	MoH	Consent opposed	No	No	No	No
BR112014005617	US2012061085	2013/059638	AbbVie	19/10/2012	Removed	10/09/2019	-	Not involved	No	No	No	No
BR112014006314	US2012061075	2013/059630	AbbVie	19/10/2012	Abandoned	22/08/2017	-	Not involved	No	No	No	No
BR112014030365	US2013044148	2013/184702	Gilead	04/06/2013	Abandoned	21/05/2019	MoH	Consent opposed	No	No	No	No
BR112014030400	US2013044138	2013/184698	Gilead	04/06/2013	Abandoned	01/08/2017	MoH	-	No	No	No	No
BR112014011938	US2014013953	2014/120981	Gilead	30/01/2014	Granted and valid	16/03/2021	MoH	Consent opposed	No	Yes	No	No

Table B.7. Patent landscape for ombitasvir used for HCV treatment in Brazil

Application	Priority	WO	Harmonised patentee	Filing date	Outcome	Outcome date	Fast-tracking	Anvisa	Third-party opposition	Appeal	Litigation	Backlog Plan
PI1004894	US2010038077	2010/144646	AbbVie	10/06/2010	Granted and valid	23/03/2021	-	Not involved	No	No	No	Yes
BR112012022774	US2011027511	2011/112558	AbbVie	08/03/2011	Abandoned	28/01/2020	-	Not involved	No	No	No	Yes
BR112012030014	NL2011050366	2011/149349	Neurophyxia	26/05/2011	Granted and valid	13/07/2021	-	Not involved	No	No	No	Yes
BR112012031500	US2011039769	2011/156578	AbbVie	09/06/2011	Abandoned	13/04/2021	-	Not involved	No	No	No	No
BR112015033022	US2014045054	2015/002952	AbbVie	01/07/2014	Abandoned	04/05/2021	-	Not involved	No	No	No	No
PI1004894	US2010038077	2010/144646	AbbVie	10/06/2010	Granted and valid	23/03/2021	-	Not involved	No	No	No	No
BR112012022774	US2011027511	2011/112558	AbbVie	08/03/2011	Abandoned	28/01/2020	-	Not involved	No	No	No	No
BR112012030014	NL2011050366	2011/149349	Neurophyxia	26/05/2011	Granted and valid	13/07/2021	-	Not involved	No	No	No	No
BR112012031500	US2011039769	2011/156578	AbbVie	09/06/2011	Abandoned	13/04/2021	-	Not involved	No	No	No	No

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Table B.8. Patent landscape for pibrentasvir used for HCV treatment in Brazil

Application	Priority	WO	Harmonised patentee	Filing date	Outcome	Outcome date	Fast-tracking	Anvisa	Third-party opposition	Appeal	Litigation	Backlog Plan
BR112013005701	US2011056045	2012/051361	AbbVie	12/10/2011	Granted and valid	10/05/2022	-	Abolished	No	No	No	Yes
BR112015006037	US2013060103	2014/047039	AbbVie	17/09/2013	Granted and valid	17/05/2022	-	Abolished	No	No	No	Yes
BR112015020918	US2014027556	2014/152635	AbbVie	14/03/2014	Abandoned	28/12/2021	-	Abolished	No	No	No	Yes
BR112015023017	US2014027423	2014/152514	AbbVie	14/03/2014	Granted and valid	30/08/2022	-	Abolished	No	No	No	Yes
BR112016022858	US2015023922	2015/153792	AbbVie	01/04/2015	Abandoned	03/11/2021	-	Restricted consent	No	No	No	Yes
BR112016022976	US2015023923	2015/153793	AbbVie	01/04/2015	Rejected	20/09/2022	-	Abolished	No	No	No	Yes
BR112017028185	US2016039266	2016/210273	AbbVie	24/06/2016	Rejected pending appeal	31/10/2023	-	Abolished	No	Yes	No	Yes
BR112018000982	US2016042806	2017/015211	AbbVie	18/07/2016	Rejected	27/06/2023	-	Abolished	No	No	No	Yes
BR102018002956	US2015431906	-	AbbVie	15/02/2018	Abandoned	03/01/2023	-	Abolished	No	No	No	Yes

Table B.9. Patent landscape for ritonavir used for HCV treatment in Brazil

Application	Priority	WO	Harmonised patentee	Filing date	Outcome	Outcome date	Fast-tracking	Anvisa	Third-party opposition	Appeal	Litigation	Backlog Plan
BR112012022774	US2011027511	2011/112558	AbbVie	08/03/2011	Abandoned	28/01/2020	-	Restricted consent	No	No	No	Yes
BR112012031500	US2011039769	2011/156578	AbbVie	09/06/2011	Abandoned	13/04/2021	-	Interrupted	No	No	No	No
BR112015033022	US2014045054	2015/002952	AbbVie	01/07/2014	Abandoned	04/05/2021	-	Interrupted	No	No	No	No

Table B.10. Patent landscape for simeprevir used for HCV treatment in Brazil

Application	Priority	WO	Harmonised patentee	Filing date	Outcome	Outcome date	Fast-tracking	Anvisa	Third-party opposition	Appeal	Litigation	Backlog Plan
PI0506945	SE2005000096	2005/073216	Medivir	28/01/2005	Abandoned	17/04/2018	MoH	Consent opposed	No	No	No	No
PI0506948	SE2005000097	2005/073195	Medivir	28/01/2005	Granted but lapsed on 23/02/2021	18/09/2018	MoH	Consent opposed	No	No	No	No
BR122018073873	EP2006064820	2007/014926	J&J; Medivir	28/07/2006	Rejected	05/01/2021	-	Consent opposed	No	No	No	No
PI0614654	EP2006064820	2007/014926	J&J; Medivir	28/07/2006	Granted but lapsed on 24/09/2020	12/03/2019	MoH	Consent opposed	No	No	No	No
PI0806853	EP2008051269	2008/092955	J&J	01/02/2008	Granted but lapsed on 26/11/2019	20/03/2018	MoH	Consent opposed	No	No	No	No
PI0806945	EP2008051268	2008/092954	J&J	01/02/2008	Rejected	05/06/2018	MoH	Consent opposed	No	No	No	No

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Application	Priority	WO	Harmonised patentee	Filing date	Outcome	Outcome date	Fast-tracking	Anvisa	Third-party opposition	Appeal	Litigation	Backlog Plan
PI0919404	EP2009062096	2010/031829	Ortho-McNeil-Janssen	18/09/2009	Abandoned	19/04/2016	-	-	No	No	No	No
PI0923393	EP2009067715	2010/072742	Ortho-McNeil-Janssen	22/12/2009	Granted but lapsed on 15/10/2019	19/06/2018	MoH	Consent opposed	No	No	No	No
PI1008918	EP2010001197	2010/097229	Ortho-McNeil-Janssen	26/02/2010	Rejected	05/06/2018	MoH	Consent opposed	No	No	No	No
BR112012023296	EP2011053957	2011/113859	J&J	16/03/2011	Granted but lapsed on 14/01/2020	03/07/2018	MoH	Consent opposed	No	No	No	No
BR112012026016	EP2011055836	2011/128378	J&J; Medivir	13/04/2011	Abandoned	01/03/2017	MoH	Not involved	No	No	No	No
BR112014006984	EP2012068593	2013/041655	J&J	21/09/2012	Abandoned	16/07/2019	-	Not involved	No	No	No	No
BR112014005617	US2012061085	2013/059638	AbbVie	19/10/2012	Removed	10/09/2019	-	Not involved	No	No	No	No
BR112014006314	US2012061075	2013/059630	AbbVie	19/10/2012	Abandoned	22/08/2017	-	Not involved	No	No	No	No
BR112014009849	IB2012055900	2013/061285	J&J	26/10/2012	Abandoned	27/08/2019	MoH	Interrupted	No	No	No	No
BR112015003913	IB2013058138	2014/033668	J&J	30/08/2013	Abandoned	26/06/2018	-	Interrupted	No	No	No	No

Table B.11. Patent landscape for sofosbuvir used for HCV treatment in Brazil

Application	Priority	WO	Harmonised patentee	Filing date	Outcome	Outcome date	Fast-tracking	Anvisa	Third-party opposition	Appeal	Litigation	Backlog Plan
BR122016003746	US2001016671	2001/090121	Idenix; University of Cagliari	23/05/2001	Rejected	26/12/2018	-	Consent opposed	Yes	Yes	No	No
PI0111127	US2001016671	2001/090121	Idenix; University of Cagliari	23/05/2001	Rejected	05/06/2018	MoH	Consent opposed	Yes	Yes	No	No
PI0312286	IB2003003246	2004/002999	CNRS; Idenix; University of Cagliari; University of Montpellier 2	27/06/2003	Rejected	05/06/2018	MoH	Consent opposed	Yes	Yes	No	No
BR122018015050	US2004012472	2005/003147	Gilead	21/04/2004	Granted and valid	13/07/2021	-	Forced consent	Yes	No	Yes	No
BR122019018265	US2004012472	2005/003147	Gilead	21/04/2004	Abandoned	15/10/2019	-	-	No	Yes	No	No
PI0410846	US2004012472	2005/003147	Gilead	21/04/2004	Granted and valid	15/01/2019	MoH	Forced consent	Yes	No	Yes	No
PI0419342	US2004012472	2005/003147	Gilead	21/04/2004	Rejected	30/01/2018	MoH	Forced consent	Yes	No	Yes	No
PI0419343	US2004012472	2005/003147	Gilead	21/04/2004	Rejected	06/02/2018	MoH	Forced consent	Yes	No	Yes	No

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Application	Priority	WO	Harmonised patentee	Filing date	Outcome	Outcome date	Fast-tracking	Anvisa	Third-party opposition	Appeal	Litigation	Backlog Plan
PI0419344	US2004012472	2005/003147	Gilead	21/04/2004	Rejected	06/02/2018	MoH	Forced consent	Yes	No	Yes	No
PI0419345	US2004012472	2005/003147	Gilead	21/04/2004	Granted and valid	22/12/2020	MoH	Forced consent	Yes	Yes	Yes	No
PI0809654	US2008058183	2008/121634	Gilead	26/03/2008	Rejected	02/05/2018	MoH	Forced consent	Yes	Yes	Yes	No
PI0823519	US2008058183	2008/121634	Gilead	26/03/2008	Rejected	21/08/2018	MoH	Forced consent	Yes	No	Yes	No
BR122013007556	US2010035641	2010/135569	Gilead	20/05/2010	Rejected	28/08/2018	MoH	Consent opposed	Yes	Yes	No	No
PI1012781	US2010035641	2010/135569	Gilead	20/05/2010	Rejected	17/04/2018	MoH	Consent opposed	No	No	No	No
BR112012024884	US2011030762	2011/123668	Gilead	31/03/2011	Abandoned	02/05/2017	MoH	-	No	No	No	No
BR112012024923	US2011030725	2011/123645	Gilead	31/03/2011	Rejected	03/07/2018	MoH	Consent opposed	Yes	Yes	No	No
BR122013004621	US2011030725	2011/123645	Gilead	31/03/2011	Rejected	10/12/2019	MoH	Consent opposed	Yes	No	No	No
BR112013001267	US2011044581	2012/012465	Gilead	19/07/2011	Rejected	26/02/2019	MoH	Consent opposed	Yes	No	No	No
BR112014006324	US2012055621	2013/040492	Gilead	14/09/2012	Granted and valid	26/12/2018	MoH	Consent opposed	No	No	No	No
BR112014005617	US2012061085	2013/059638	AbbVie	19/10/2012	Removed	10/09/2019	-	Not involved	No	No	No	No
BR112014006314	US2012061075	2013/059630	AbbVie	19/10/2012	Abandoned	22/08/2017	-	Not involved	No	No	No	No
BR112014010295	US2012062115	2013/066748	Gilead	26/10/2012	Abandoned	02/05/2017	-	Not involved	No	No	No	No
BR112014012739	US2012066605	2013/082003	Gilead	27/11/2012	Rejected	06/07/2021	-	Consent opposed	Yes	No	No	No
BR122020025134	US2012066605	2013/082003	Gilead	27/11/2012	Rejected	06/07/2021	-	Consent opposed	Yes	No	No	No
BR112014011938	US2014013953	2014/120981	Gilead	30/01/2014	Granted and valid	16/03/2021	MoH	Consent opposed	No	Yes	No	No
BR112016003644	US2014013930	2015/030853	Gilead	30/01/2014	Rejected pending appeal	26/05/2020	-	Consent opposed	No	Yes	Yes	No
BR112016013714	US2014069123	2015/099989	Gilead	08/12/2014	Abandoned	04/10/2022	-	Abolished	Yes	No	No	No

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Table B.12. Patent landscape for velpatasvir used for HCV treatment in Brazil

Application	Priority	WO	Harmonised patentee	Filing date	Outcome	Outcome date	Fast-tracking	Anvisa	Third-party opposition	Appeal	Litigation	Backlog Plan
BR112014005617	US2012061085	2013/059638	AbbVie	19/10/2012	Removed	10/09/2019	-	Not involved	No	No	No	No
BR112014006314	US2012061075	2013/059630	AbbVie	19/10/2012	Abandoned	22/08/2017	-	Not involved	No	No	No	No
BR112013012091	US2012065681	2013/075029	Gilead	16/11/2012	Rejected	09/03/2021	Infraction	Consent opposed	Yes	Yes	No	No
BR112016003644	US2014013930	2015/030853	Gilead	30/01/2014	Rejected pending appeal	26/05/2020	Technology	Consent opposed	No	Yes	Yes	No
BR112016028773	US2015034655	2015/191437	Gilead	08/06/2015	Granted and valid	07/02/2023	-	Restricted consent	No	No	No	Yes
BR112016028843	US2015034649	2015/191431	Gilead	08/06/2015	Abandoned	24/09/2020	-	Restricted consent	No	No	No	No

Table B.13. Patent landscape for veruprevir used for HCV treatment in Brazil

Application	Priority	WO	Harmonised patentee	Filing date	Outcome	Outcome date	Fast-tracking	Anvisa	Third-party opposition	Appeal	Litigation	Backlog Plan
BR122012005261	US2009005082	2010/030359	AbbVie; Enanta	10/09/2009	Abandoned	05/10/2021	-	Restricted consent	No	No	No	No
PI0918724	US2009005082	2010/030359	AbbVie; Enanta	10/09/2009	Granted and valid	03/12/2019	-	Restricted consent	No	No	No	No
BR112012022774	US2011027511	2011/112558	AbbVie	08/03/2011	Abandoned	28/01/2020	-	Restricted consent	No	No	No	Yes
BR112012031500	US2011039769	2011/156578	AbbVie	09/06/2011	Abandoned	13/04/2021	-	Interrupted	No	No	No	No
BR112015033022	US2014045054	2015/002952	AbbVie	01/07/2014	Abandoned	04/05/2021	-	Interrupted	No	No	No	No

Appendix C: centralised tenders for HCV drugs in Brazil

This Appendix summarises the negotiation of the six tenders for HCV drugs. For each tender, a table indicates the purchasing volume, the maximum price, which sellers joined the process, their first and final offers, and the winning offer. Here, all prices are presented in current values. The first and fourth tenders, both limited to a single drug, were the only ones where the purchase units were drugs. In the others, the MoH procured units of full treatments.

Table C.1. Summary of the first tender (87/2018)

Group	Drug units	Maximum price	Offer	SOF		
				Gilead	Hospinova	Maxima
1	1,160,880	32.86	First	89.7043	170.00	3,000.00
			Final	89.7043	**32.86**	63.92

Note: The acronym SOF is used for sofosbuvir. The value in bold was the winning offer. Prices are rounded up to two decimals.

Table C.2. Summary of the second tender (105/2018)

Group	Treatment units	Maximum price	Offer	DAC	SOF		LED/SOF	VEL/SOF	ELB/GRA	GLE/PIB
				Swords	Blanver	Gilead	Gilead	Gilead	MSD	AbbVie
1	29,574	4,827.19	First	2,287.41	-	4,253.67	4,253.67	5,446.20	-	24,081.85
			Final	2,287.41	-	4,253.67	**4,253.67**	5,446.20	-	24,081.85
2	1,231	7,759.73	First	12,004.70	8,190.00	10,291.39	9,056.42	10,085.56		
			Final	12,004.70	4,032.00	-	**4,253.67**	10,085.56		
3	10,535	6,158.52	First	9,515.60	6,491.88	8,157.55		6,723.71		29,730.68
			Final	9,515.60	3,530.00	-		**5,446.20**		29,730.68
4	406	3,975.33	First	11,773.13	4,422.60	5,557.35		5,446.20	12,967.08	24,081.85
			Final	11,773.13	4,422.60	5,557.35		5,446.20	12,967.08	24,081.85
5	454	9,915.21	First	27,868.90	10,469.01	13,155.14		12,892.05		
			Final	27,868.90	10,469.01	-		**5,446.20**		
6	2,103	4,827.19	First						25,405.03	34,402.64
			Final						17,427.85	34,402.64
7	842	8,792.11	First	29,069.47	10,920.00	13,721.85	12,075.23	13,447.41		29,730.68
			Final	29,069.47	10,920.00	13,721.85	**4,253.67**	5,446.20		29,730.68
8	311	8,792.11	First	29,069.47	10,920.00	13,721.85		13,447.41		29,730.68
			Final	29,069.47	10,920.00	13,721.85		**5,446.20**		29,730.68

Note: Acronyms are used for drug names: daclatasvir (DCV), elbasvir (ELB), ledipasvir (LED), glecaprevir (GLE), grazoprevir (GRA), pibrentasvir (PIB), sofosbuvir (SOF), and velpatasvir (VEL). Values in bold were the winning offers for each group. Blank spaces indicate when the drug was not recommended for that group, and hyphens indicate when the sellers did not place any offer or when they abandoned the competition. Vertical lines separate regimens for easier comparison.

Table C.3. Summary of the third tender (56/2020)

Group	Treatment units	Maximum price	Offer	LED/SOF Gilead	VEL/SOF Gilead	ELB/GRA	GLE/PIB
1	33,690	4,721.07	First	15,167.35	17,160.00	-	-
			Final	**6,306.28**	17,160.00	-	-
2	1,810	4,721.07	First	30,568.04	33,466.73		
			Final	**6,306.28**	33,466.73		
3	13,477	6,044.64	First		17,160.00		-
			Final		**8,050.00**		-
4	285	6,044.64	First		17,160.00	-	-
			Final		**8,050.00**	-	-
5	738	6,044.64	First		33,482.93		
			Final		**8,050.00**		

Note: : Acronyms are used for drug names: elbasvir (ELB), ledipasvir (LED), glecaprevir (GLE), grazoprevir (GRA), pibrentasvir (PIB), and velpatasvir (VEL). The values in bold were the winning offers for each group. Blank spaces indicate when the drug was not recommended for that group or when no seller joined the tender. Vertical lines separate regimens for easier comparison.

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Table C.4. Summary of the fourth tender (161/2021)

Group	Drug units	Maximum price	Offer	SOF
				Blanver
1	54,292	38.27	First	300.00
			Final	89.70

Note: There was no suitable offer. Prices were rounded up to two decimals.

Table C.5. Summary of the fifth tender (28/2022)

Group	Treatment units	Maximum price	Offer	DAC	SOF		VEL/SOF	GLE/PIB
					Blanver	Gilead	Gilead	
1	47,307	6,602.64	First	-	7,736.40	-	8,050.00	-
			Final	-	7,736.40	-	8,050.00	-
2	1,994	6,602.64	First	-	7,736.40	-	16,100.00	
			Final	-	7,736.40	-	7,230.00	

Note: Acronyms are used for drug names: daclatasvir (DCV), ledipasvir (LED), glecaprevir (GLE), pibrentasvir (PIB), sofosbuvir (SOF), and velpatasvir (VEL). There was no suitable offer for any group. Blank spaces indicate when the drug was not recommended for that group or when no seller joined the tender, and hyphens indicate when the sellers did not place any offer. Vertical lines separate regimens for easier comparison.

Table C.6. Summary of the sixth tender (78/2022)

Group	Treatment units	Maximum price	Offer	VEL/SOF		GLE/PIB
				Elfa	Gilead	
1	47,307	7,230.00	First	87,995.04	7,230.00	-
			Final	87,995.04	**7,160.00**	-

Note: Acronyms are used for drug names: glecaprevir (GLE), pibrentasvir (PIB), sofosbuvir (SOF), and velpatasvir (VEL). The values in bold were the winning offers for each group. Blank spaces indicate when no seller joined the tender, and hyphens indicate when the sellers did not place any offer. Vertical lines separate regimens for easier comparison.