Ministério da Saúde

FIOCRUZ
Fundação Oswaldo Cruz

ESCOLA NACIONAL DE SAÚDE PÚBLICA SERGIO AROUCA ENSP

# Mercosur-EU Free Trade Agreement: Impact analysis of TRIPS-plus measures proposed by the EU on public purchases and domestic production of HIV and Hepatitis C medicines in Brazil

September 2017

Authors[i]
Gabriela Costa Chaves – researcher, Sergio Arouca National School of Public Health, Oswaldo Cruz Foundation (ENSP/Fiocruz)
Walter Britto Gaspar – research assistant, Sergio Arouca National School of Public Health, Oswaldo Cruz Foundation (ENSP/Fiocruz)
Marcela Fogaça Vieira – legal advisor, consultant Shuttleworth Foundation

This study is part of the "AccessIBSA project" coordinated by Achal Prabhala and funded by the Shuttleworth Foundation.



[i] The authors would like to thank Dr. Joan Rovira and Miguel Cortes, developers of the IPRIA Model, for their valuable advice, review and comments on the application Model that was used in this study to estimate the impact of changes in intellectual property regulations. However, the authors are responsible for the collection and selection of the data used to feed the Model and for running it, as well as for all the assumptions made along the study and are solely responsible for the results, analysis and police recommendations made in this report.

## Table of contents

## Charts

## Figures

**Executive Summary**

The Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) of the World Trade Organization (WTO) established the obligation to recognise patent rights in all technological fields. Patents guarantee a period of exclusivity in the market by excluding the participation of third parties in the different stages involving production and trade. In the absence of substitutes/competitors, market exclusivity provides a monopolistic position that allows the power to set prices often very much higher than in a scenario with competition. In the pharmaceutical sector, patents have an impact on access and production of medicines and other technologies, with direct implication on public policies related to health and industrial development.

The TRIPS Agreement contains provisions that need to be applied by all WTO country members. Members are not required to provide more extensive protection than is required by TRIPS, but they are allowed to negotiate such provisions (known as TRIPS-plus) outside the WTO multilateral forum. The European Union (EU) and Mercosur countries are currently negotiating a free trade agreement (FTA) containing a chapter on intellectual property rights (IPR).

In the end of 2015, the former United Nation Secretary-General convened a High-Level Panel on Access to Medicines to address the policy incoherence between the justifiable rights of inventors, international human rights law, trade rules and public health in the context of health technologies. One of the many conclusions and recommendations of the final report released in September 2016 was for the development of public health impact assessments by governments engaged in trade and investment treaties in order to assure that these agreements do not include provisions that interfere with their obligations to fulfil the right to health.

The present study aims to contribute to the assessment of the public health impact of the Mercosur-EU FTA by estimating the impact of TRIPS-plus measures proposed by the EU on public expenditures on medicines and sales of domestic production in Brazil. In this report, we present findings related to the antiretroviral (ARV) medicines used in the treatment of HIV/Aids and to the medicines used for hepatitis C.

Previously, in March 2017, a preliminary report of the study was released. That report analysed the EU proposal for the IPR chapter that was made publicly available in September 2016. The preliminary report identified three main TRIPS-plus provisions with implications for health policies: (i) mandatory adoption of regional or national exhaustion of intellectual property rights (IPR); (ii) extension of the period of protection conferred by a patent on medicinal products and (iii) exclusivity of data submitted to obtain market authorization. The preliminary report also made an

estimation of the impact of one of those TRIPS-plus measures – patent term extension - on prices of selected medicines in Brazil. The calculations included six medicines that may have their patent protection extended under such provision: three for HIV (darunavir, etravirine, raltegravir); two for Hepatitis C (sofosbuvir, daclatasvir); one for cancer (dasatinib). It was estimated that this extension would represent an **additional expenditure of nearly USD 444 million by the Brazilian Ministry of Health (MoH),** in comparison with the lowest international prices.

In this report, we present the findings of a more comprehensive impact assessment of two of the TRIPS-plus provisions contained in the EU proposal: patent term extension and data exclusivity. As Brazilian law already adopts the national regime of exhaustion of IPR, the impact of that specific provision was not individually calculated in the study, even though it is considered in the base scenario. We applied the Intellectual Property Rights Impact Aggregate (IPRIA) Model[i] in order to estimate the impact of such provisions on the public expenditures and domestic sales of medicines in Brazil, taking the reality of the Brazilian market as a base for the calculations.

The Model was applied only to the market segment comprised by ARV medicines indicated for the treatment of HIV and to the market segment of medicines for hepatitis C, which are both exclusively public in Brazil. It was not applied to estimate the impact of IPR changes in the Brazilian pharmaceutical market as a whole, as was done in most of the other studies conducted to estimate the impact of TRIPS-plus provisions in health. The results should be read considering this.

The selection of the two case studies took into consideration the significant difference between them. In Brazil, the ARV market has been relatively stable over the past years in terms of public expenditures and included an important share of generic medicines, both imported and locally produced, mostly as a result of adoption of measures to challenge patent barriers (threat and issue of compulsory license, patent oppositions, experimental use/Bolar exception and voluntary license).

On the other hand, the hepatitis C market has been sharply increasing; it is historically almost 100% under exclusivity. The strategies adopted to try to remove IPR barriers had not yet fully resulted in changes in the market as of 2016, resulting in a market in which the negative impact of IPR on public expenditures and local production can be measured in full.

---

[i] Guide to the IPRIA (Intellectual Property Rights Impact Aggregate) Model (2009). Available at https://www.ictsd.org/sites/default/files/event/2010/03/guide-to-the-ipria-model.pdf

For these reasons we consider the ARV market and the hepatitis C market to be key case studies to simulate and illustrate the implications on public expenditures and sales by domestic producers with the adoption of TRIPS-plus provisions proposed by the EU in the FTA negotiations with Mercosur.

The IPRIA model is based on a "scenario methodology": a base scenario, which reflects the market behaviour based on the selected parameters as well as the effects of legislation/regulation that has been already approved at the initial year of the period analysed, is compared with alternative scenarios that incorporate the impact of the potential changes on IPR taking into account the behaviour of the Brazilian market. The study considered two main outcomes: (i) **changes in public expenditures** and (ii) **changes in the sales of domestic producers**. The latest was only calculated for the ARV market, as the sales of domestic producers in the hepatitis C market in Brazil are only residual and represent around 0.01% of sales.

We used the prospective simulation to produce five different scenarios in order to estimate the impact of the inclusion of each of the above-mentioned TRIPS-plus provisions proposed by the EU both separately and together.

i. Base scenario – the evolution of the market if there are no changes on IP regulations in Brazil, therefore including TRIPS-plus provisions already adopted in Brazilian law;
ii. Alternative scenario 1 – the evolution of the market in the absence of the article 40, sole paragraph, of the current Brazilian patent law, which allows for patent term extension based on patent examination delay;
iii. Alternative scenario 2 – the evolution of the market in the case of adoption of patent term extension as a consequence of market authorization delay;
iv. Alternative scenario 3 – the evolution of the market in the case of adoption of data exclusivity for a period of 5 and 8 years;
v. Alternative scenario 4 – the adoption of both data exclusivity (5 and 8 years) and patent term extension due to delay in regulatory market authorization.

The **<u>main results</u>** can be summarized as follows:

i. The base scenario shows that without any change in the IP legislation:
    a. The ARV expenditures would go from BRL 1.12 billion in 2015 to BRL 2.95 billion in 2050, considering the trend of growth of 3% (adjusted for the inflation) observed from 2008-2015 (Chart 24).
    b. The hepatitis C expenditures would go from BRL 1.024 billion in 2016 to BRL 2.05 billion in 2051. This was calculated using the very conservative market growth of 2% observed from 2015-2016 (Chart 25).

ii. Alternative scenario 1 shows that if Brazilian industrial property legislation were changed to remove the patent term extension due to patent examination delay:
    a. For ARV, there would be savings of BRL 2.05 billion by the Brazilian MoH in the period of 2015 – 2050 (an average of BRL 58.7 million per year). It would also lead to an increase in the sales of domestic producers of BRL 92.3 million (Chart 26).
    b. For hepatitis C, the savings in public expenditures would be of BRL 16.32 billion in the period from 2016-2051, a simple average of BRL 481.7 million per year (Chart 27).

iii. Alternative scenario 2 shows that the adoption of the patent term extension due to market authorization delay as proposed by the EU would lead to:
    a. For ARV, an additional expenditure of BRL 1.25 billion by the Brazilian MoH in the period of 35 years (an average of BRL 35.8 million per year). It would also lead to a decrease in the sales of domestic producers of BRL 102 million (Chart 28).
    b. For hepatitis C, it would lead to additional expenditures of BRL 16.3 billion (an average of BRL 466.4 million) (Chart 29).

iv. Alternative scenario 3 shows that the adoption of data exclusivity would lead to:
    a. For ARV, an additional expenditure by the Brazilian MoH in the period of 2015-2050 of BRL 2.42 billion if it was adopted for a period of 5 years (an average of BRL 70.1 million per year) or of BRL 3.74 billion if adopted for a period of 8 years (an average of BRL 106.8 million per year). It would also lead to a decrease in the sales of domestic producers in the same period of BRL 237.06 million if adopted for 5 years or BRL 423.7 million if adopted for 8 years (Chart 30).
    b. For hepatitis C, there would be an additional expenditure of BRL 31.45 billion from 2016-2051, an average of BRL 898.6 million per year (5 years data exclusivity); and, BRL 47.8 billion from 2016-2050, an average of BRL 1.37 billion per year (8 years data exclusivity) (Chart 31).

v. Alternative scenario 4 shows that the adoption of both TRIPS-plus provisions proposed by the EU would lead to:
    a. For ARV, an additional expenditure by the Brazilian MoH in the period of 2015-2050 of BRL 3.7 billion if data exclusivity was adopted for a period of 5 years (an average of BRL 105.9 million per year) or of BRL 4.99 billion if adopted for a period of 8 years (an average of BRL 142.7 million per year). It would also lead to a decrease in the sales of domestic

producers in the same period of BRL 393 million if adopted for 5 years or BRL 612 million if adopted for 8 years (Chart 32).

b. For hepatitis C, there would be additional expenditures of BRL 46.6 billion in the accumulative from 2016-2051, an average of BRL 1.33 billion per year (5 years data exclusivity); and, BRL 63 billion in the accumulative from 2016-2051, an average of BRL 1.8 billion per year (8 years data exclusivity) (Chart 33).

**Chart 1 - Summary of the findings**

| Scenario | Time period | Variation in ARV expenditure compared to base scenario (BRL) | Variation in expenditure on medicines for hepatitis C compared to base scenario (BRL) |
|---|---|---|---|
| Alternative (Alt) 1 | 2015-2050 for ARV and 2016-2051 for hepatitis C | -2,054,436,157.85 | -16,862,109,838.52 |
| Alt 2 | | 1,255,011,241.61 | 16,326,989,040.47 |
| Alt 3 (5-years DE) | | 2,452,784,149.22 | 31,451,189,948.91 |
| Alt 3 (8-years DE) | | 3,740,179,503.19 | 47,861,780,962.03 |
| Alt 4 (5-years DE) | | 3,707,795,390.84 | 46,639,086,730.75 |
| Alt 4 (8-years DE) | | 4,995,190,744.80 | 63,049,677,743.86 |

The **discussion of the results** highlights the implications that changing the industrial property law could have for policies of access to health and national development, summarized below:

(i) The public expenditures on ARV in Brazil have been relatively stable in the past years as a result of multiple strategies adopted to negotiate price and remove patent barriers, such as the use of public health TRIPS flexibilities, allowing for the treatment of more people with small increase in total expenditures;

(ii) The hepatitis C market in Brazil is almost 100% under exclusivity between 2006 to 2016. Only patent oppositions have been presented for sofosbuvir and daclatasvir and results have not shown full result yet. Public expenses have been increasing and treatment has not been available to all in need. The impact of exclusive rights is higher in hepatitis C than in ARV as of today and will be even worse if more exclusive rights are adopted in the country;

(iii) The adoption of the TRIPS-plus measures proposed by the EU, besides the increase in public expenditures on medicines and reduction of domestic

sales shown in the study, would also reduce the policy space currently available to adopt measures to reduce the negative impact of IPR on health policies, such as the TRIPS flexibilities. That could lead to even higher increase in public expenditures and decrease of sales by national producers in the whole pharmaceutical market;

(iv) The removal of already existing TRIPS-plus provision that extends the market exclusivity due to patent term extension would lead to savings of public money and increase in domestic sales;

(v) Public expenditures on medicines have been increasing in the past years, consuming rising shares of the total public health budget as a result of incorporating medicines under market exclusivity. Therefore, the adoption of new measures that increase market exclusivity is detrimental to the sustainability of the public health system.

Based on the results and discussions of the study, the authors make the following **recommendations:**

1. The non-adoption of any TRIPS-plus provision that extends market exclusivity as proposed by the European Union in the negotiation of the Free Trade Agreement with Mercosur, considering the negative impact of those measures on policies of access to health and national development in Brazil;
2. For the Brazilian government and other countries involved in the negotiation of the FTA to conduct an impact study in the field of public health and human rights, as recommended recently by the UN High-Level Panel on Access to Medicines. The impact studies should be conducted transparently and be made publicly available;
3. The negotiations of the FTA should be transparent and all draft texts and proposals from all parties involved should be publicly disclosed and public consultations should be held to allow the participation of all sectors of society;
4. For the Brazilian government to make all efforts necessary to exclude TRIPS-plus measures already foreseen in national IP legislation, especially the removal of the provision included in the sole paragraph of article 40 of the patent law that allows for patent term extension due to delay in patent examination.

## Introduction

The WTO TRIPS Agreement, which came into effect on 1 January 1995, changed the international system of intellectual property with the establishment of minimum protection standards. This Agreement significantly changed the levels of protection practised in developing countries, raising them, in most cases, to levels incompatible with their own stages of development[1].

Resulting from an intensely private agenda, coordinated by a group of multinational companies[ii], and led by developed nations such as the United States, Japan and some European countries[2], the TRIPS Agreement established the obligation to grant patent protection in all technological fields for a minimum duration of 20 years by all member members of the WTO. The Agreement does, however, factor in varying implementation deadlines (transition periods), according to the development classification of the member countries, a period not always fully enjoyed by the respective countries.

The negotiations of the Agreement did not occur without resistance from developing countries, which sought to minimise the negative impact by adopting provisions that would balance intellectual property rights abuses[1]. But for those who advocate the strengthening of global standards of intellectual property protection, the TRIPS Agreement fulfilled 95% of their expectations[3].

The TRIPS Agreement was regarded as setting out the minimum standards for intellectual property protection, opening a window of opportunity to even higher standards – the other 5% – to be negotiated outside the WTO multilateral forum and in a context of increased asymmetry among countries involved. The so-called 'TRIPS-plus provisions' are those that go beyond the TRIPS Agreement, as a rule, strengthening the power conferred by intellectual property and restricting the space for the adoption of measures that minimise the effects arising from the abuse of monopoly powers awarded by intellectual property.

For the pharmaceutical sector, and especially multinational pharmaceutical companies, the protection of intellectual property is a key instrument of its commercial and innovation strategies, particularly of industrial property that includes trademarks and patents and other market exclusivity privileges. Patents guarantee companies a period

[ii] During the negotiations of the TRIPS Agreement, in the Uruguay Round of GATT, the Intellectual Property Committee (IPC) advised the United States, in conjunction with other developed countries. The IPC was composed of the following companies: Bristol-Myers, CBS, Du Pont, General Electrics, General Motors, Hewlett-Packard, IBM, Johnson & Johnson, Merck, Monsanto, Pfizer (Sell, 2003).

of exclusivity in the market for their products, excluding third parties, without their consent, from the different stages involving production and trade. In the absence of substitutes/competitors, market exclusivity provides a monopolistic position that allows them the power to set prices often much higher than in a scenario with competition. This privilege is justified on the ground that it is required to recover their alleged cost on research and development (R&D). The argument goes on stating that without strong IPR there would be no R&D and hence no future innovation to address existing health needs. Branding contributes to product differentiation market strategies, which together with other strategies aimed at influencing prescription patterns, contribute to strengthening dominant market positions during and after the exclusivity period and, ultimately, to increased sales for these products[4].

More recently, cases such as that of the new medicine sofosbuvir, a drug that can cure chronic hepatitis C (above 90% efficacy rate) - initially marketed at USD 1,000 per tablet - as well as oncological medicines marketed at exorbitant prices, often unaffordable and financially unsustainable even to the health systems of the wealthiest countries, rekindled the debate on the limits of intellectual property protection in the face of lack of access to medicines that have the potential to save millions of lives[5-8].

On the other hand, the TRIPS Agreement also contains provisions that make it possible to safeguard public health, the so-called 'TRIPS flexibilities of public health protection', which allows for the removal of the exclusivity conferred by intellectual property rights. This allows for the entry of generic medicines, enabling competition to encourage price reductions[9,10]. In 2001, the "Doha Declaration on the TRIPS agreement and public health", adopted in the WTO framework, reaffirmed the right of countries to adopt such measures of public health protection.

At the international level, different organisations recommend caution with the adoption of TRIPS-plus provisions, as they may have a negative impact on the ability of states to provide essential medicines, a component of the obligation of the state for the realisation of the human right to health. Recently, in September 2016, a report was published by the United Nations Secretary-General's High-Level Panel on Access to Medicines that had, among its recommendations, a recommendation to countries to conduct preliminary public health impact studies[11] while negotiating trade agreements.

***The Mercosur-EU FTA***

Negotiations on a trade agreement between the European Union and Mercosur began in the year 2000. Intensive negotiations were held in 2004 with the objective of concluding the agreement by the end of that year. However, in October 2004, at a ministerial meeting in Lisbon, Portugal, both parties agreed that they would need more time to draft the agreement and the negotiations were suspended. In May 2010, negotiations were officially resumed and since then 28 rounds of negotiations have taken place (including the Bi-regional Negotiating Committee Meeting - BNC). The latest round with Mercosur was held in July 2017 in Brussels and the next one is planned to take place in Brasilia from 2 to 6 of October 2017.

The aim is to negotiate a comprehensive trade agreement covering not only trade in industrial and agricultural goods but also services and public procurement, as well as intellectual property and other technical barriers to trade. Unlike most trade agreement negotiations, the EU made public the text proposed for some chapters of the agreement being negotiated, including the one related to intellectual property rights[iii], which is the object of the present study.

An analysis of the last publicly available text of the EU proposal for the chapter on intellectual property (dated of 23 September 2016) shows that it includes the following TRIPS-plus provisions:

- **Exhaustion of intellectual property rights -** Article 3 of the EU proposal addresses the exhaustion of intellectual property rights. Under the proposal, the parties would either adopt the national regime, or the regional exhaustion regime. Under WTO TRIPS Agreement countries may choose the exhaustion regime they consider most appropriate (Articles 6 and 28 of the TRIPS Agreement and Article 5d of the Doha Declaration on TRIPS and Public Health). Thus, by means of TRIPS, countries may also opt for the international exhaustion regime, which would not be possible if the EU proposal was accepted.
- **Extension of the period of protection conferred by a patent on medicinal products -** According to Article 8.3 of the proposal presented by the EU, countries should extend the term of validity of a patent for a medicinal product that has undergone an administrative authorisation procedure for its commercialisation. The extension period is the period between the filing of the

[iii] Available at: http://trade.ec.europa.eu/doclib/docs/2016/november/tradoc_155070.pdf. Last accessed on 21/08/17.

patent application and the first authorisation to place the product on the national market, reduced by 5 years. In the case of medicinal products for which studies for paediatric formulations have been carried out, countries should grant a further extension of the patent term for a period not specified in the proposal text. The same provision applies to patents on phytopharmaceutical products [plant production products] (Article 8.5).

- **Exclusivity of data submitted to obtain an authorisation to put a medicinal product on the market -** In accordance with Article 10.2 of the EU proposal, the parties shall not allow any other manufacturer of the same or similar product to obtain marketing approval based on a marketing approval granted to the manufacturer who provided the results of pre-clinical or clinical tests, for a period of […] years (the number of years is not specified in the proposal). An additional period, also not specified in the proposal, would be granted in case of authorisation to one or more new therapeutic indications that may be considered of significant clinical benefit. In other FTAs signed with the EU, a minimum period of 5 years was adopted.

Previous to the FTA negotiations round held in March 2017, the Brazilian team of the "AccessIBSA project" (Shuttleworth Foundation) estimated the effects of one of the TRIPS-plus measures proposed by the EU in the IP chapter (extension of patent term) in the public expenditures by the Brazilian Ministry of Health (MoH)[iv]. That was a preliminary estimation and included only six medicines: three for HIV (darunavir, etravirine, raltegravir); two for Hepatitis C (sofosbuvir, daclatasvir); one for cancer (dasatinib). By estimating the patent extension of each selected medicine, considering the purchases made in 2015 (volume) and comparing to the prices paid by the MoH with generic versions available in the international market, it was possible to estimate an **additional expenditure of nearly USD 444 million with the adoption of only this TRIPS-plus measure during the additional monopoly time brought by the extension of the patent term of each of those six drugs**.

In order to further estimate the impact of the FTA on the public purchases of medicines in Brazil, we conducted the present impact study, which estimates the impact of two of the TRIPS-plus measures proposed by the EU (patent term extension and data exclusivity). As Brazilian law already adopts the national regime of exhaustion

[iv] For the full version of the preliminary report, please see - http://bit.ly/ftaeumercosur1 (Portuguese version) and http://bit.ly/ftaeumercosur1eng (English version).

of IPRv, the impact of that specific provision was not individually calculated in the study, even though it is considered as part of the base scenario.

There have been some estimates published on the impact of adopting TRIPS-plus provisions on the pharmaceutical market and medicines costs in Latin American countries (Colombia, Ecuador, Peru, Costa Rica and the Dominican Republic)[12-17]. These studies were based on an economic model of measuring the impact of IPR changes[18] on access to medicines. These analyses considered three main outcomes: i) changes in the consumption of medicines, ii) changes in the expenditures with medicines, and iii) changes in the domestic market share.

The present study applies the same Intellectual Property Rights Impact Aggregate (IPRIA) Model used in the above-mentioned studies to estimate the impact of the adoption of two TRIPS-plus provisions proposed by the EU both in the prices of medicines and purchases by the public health system in Brazil and the changes in the domestic market share. Initially, the model was applied only to the HIV antiretroviral (ARV) market and Hepatitis C market in Brazil that are exclusively public, as all these medicines are provided by the Unified Health System (SUS) and there are no sales in the private market. In this study, the Model was not applied to estimate the impact of IPR changes in the Brazilian pharmaceutical market as a whole, as done in most of the other studies conducted to estimate the impact of TRIPS-plus provisions in health. The results should be read considering this.

The analysis of the impact of changes in the intellectual property regulations in Brazil should take into account the fact that the Brazilian patent law already has adopted TRIPS-plus measures, with significant impact on prices of medicines as briefly described in the next section.

***The Brazilian patent legislation is already TRIPS-plus***

In relation to industrial property, Brazil passed law number 9.279/96 to comply with the TRIPS Agreement, granting patent protection for pharmaceutical products in advance as of May 1997, therefore not taking advantage of the transition period allowed under TRIPS until 2005 for developing countries. In addition, the law incorporated a series of TRIPS-plus provisions that turned out to be harmful to access

[v] The WTO TRIPS Agreement allows countries to choose the regime of exhaustion of IPR they will adopt. Brazilian patent law adopted the regime of national exhaustion of IPR (article 43), therefore restricting parallel imports. There are 2 bills ongoing at the National Congress proposing to change the regime of exhaustion of IPR to the international regime (PL 139/99 and PL 8091/2014).

policies, especially under the Unified Health System (SUS). Among the TRIPS-plus provisions adopted in the Brazilian legislation are the mechanism of patent revalidation known as "pipeline" (articles 230 and 231), which allowed for the granting of patents retrospectively, and the sole paragraph of article 40, which allows for extension of patent term due to delay in granting by the Brazilian Patent Office (INPI). Both provisions had their validity questioned under the Brazilian constitution in the Federal Supreme Court (Direct Action of Unconstitutionality – ADI 4234 and ADI 5061 and 5529, respectively, which are still awaiting decision). There are two bills – PL 139/99 and PL 8091/2014 - ongoing at the National Congress to remove the provision of the article 40 of the Brazilian patent law.

In the last twenty years, the assurance of pharmaceutical services in the public health system has represented an important step forward in terms of expanding access to medicines for the Brazilian population[19], and has also been the target of increasing challenges for the sustainability of policies on access to medicines.

These include the growing incorporation of new technologies under monopoly[20] and the growing expenditure on medicines by the federal, state and municipal levels of government[21,22]. The expenses on medicines by the Ministry of Health (the federal entity being responsible for the purchase of the most expensive technologies) went from 8.5 billion Reais (BRL) in 2008 to 14.8 billion Reais (BRL) in 2015[23].

Furthermore, it is also possible to illustrate the monetary losses to SUS caused by the above-mentioned TRIPS-plus provisions adopted by the Brazilian patent law.

In the case of patents which were revalidated under the pipeline mechanism, Hasenclever et al.[24] estimated the extra amounts that the Ministry of Health paid, compared to the purchase of generic versions for six[vi] antiretrovirals (ARV) available in the international market, in different formulations, but which were protected by pipeline patents in Brazil. Looking at the purchased volume and the difference between prices paid and prices available from two different sources (the World Health Organization – WHO and Médecins Sans Frontières - MSF) in the 2001 - 2007 period, ***the loss was estimated at approximately USD 420 million (MSF minimum prices) and USD 519 million (WHO minimum prices)***. Another study[25] estimated that from May 2009 to December 2010, the Ministry of Health spent ***an extra BRL 123 million*** on the purchase of four medicines protected by pipeline patents (imatinib, lopinavir/ritonavir,

[vi] The six ARVs analyzed were: abacavir, amprenavir, efavirenz, lopinavir/ritonavir, nelfinavir and ritonavir.

olanzapine and atorvastatin) when compared to what it would have spent on generic versions of these products.

On patent term extension, article 40 of the Brazilian patent law has a sole paragraph that allows extension of patent term in case it takes more than 10 years to be granted in the country. A study[26] identified nine medicines purchased by the Ministry of Health[vii] whose patent terms were extended or have patent applications that are pending analysis by the patent office for more than 10 years and, if granted, will have patent protection for a period of over 20 years. Based on the years of accumulated extensions up to January 2016 and the average volume of purchases of the last 3 years, the authors estimated how much more the government will pay for those nine medicines when compared to the possibility of buying generic versions and more affordable biosimilar medicines. ***The estimated amount was a total of BRL 2.14 billion or about BRL 933 million per year.***

These are some examples that illustrate the damage caused to SUS by the TRIPS-plus provisions already adopted in the Brazilian legislation, which are enough to support the understanding that these kinds of measures should not be adopted in any case in intellectual property chapters proposed in trade agreements involving Brazil. Below, we will develop on the estimation of further losses that would be caused to SUS in case the proposed TRIPS-plus provisions contained in the EU proposal are adopted.

## Methodology

### *Selection of the market in Brazil*

For the purpose of this study, we selected two case studies to estimate the impact of the IPR changes in Brazil: (i) antiretroviral (ARV) medicines used for the treatment of HIV and (ii) medicines used for the treatment of Hepatitis C. In both cases, those medicines are only supplied by the public sector in Brazil, which means there is only a public market. We did not apply the Model to estimate the impact in the Brazilian pharmaceutical market as a whole, as done in most of the other studies conducted to estimate the impact of TRIPS-plus provisions in health. This choice was based on the fact that the variables considered in the Model can vary considerably when considering

[vii] The nine medicines were: adalimumab, erlotinib, maraviroc, raltegravir, cinacalcet, sofosbuvir, trastuzumab emtansine, gefitinib, etravirine. The study considered the price difference between the Brazilian price and the lowest generic price, when available, or a 40% difference in the absence of generics in the international market.

different market segments and we wanted the figures to be more accurate according to each specific disease segment and to the public market.

The selection of the two case studies took into consideration the significant difference between them. In Brazil, the ARV market has been relatively stable over the past years in terms of expenditures. Almost 35% of the market, in terms of sales, is under exclusivity (2015) and there is domestic production of generics. The Brazilian response to the HIV/Aids epidemic has been based on the combination of prevention and care strategies, including access to treatment. Brazil was one of the first developing countries to provide access to treatment and pursued different policies to ensure the provision of those treatments, such as: local production of medicines, price negotiations with multinational companies and adoption of measures to challenge patent barriers (threat and issue of compulsory licenses, patent oppositions, experimental use/Bolar exception and voluntary license)[27]. As a consequence of those initiatives, the public expenditures on ARV have been kept relatively stable in face of the increase in the number of patients starting and under treatment [28, 29].

It should be noted, however, that it is unlikely this scenario will continue to be stable, as in 2013 the treatment guideline has changed to treat all people living with HIV[30], which is expected to increase the number of people in treatment beyond variation in previous years, and because the newer ARV are under exclusivity and are replacing current ARV with generic alternatives. Considering that the first ARV were produced in Brazil due to the lack of grant of patents for pharmaceuticals before 1996, it should be expected that the proportion of the medicines under exclusivity should increase in relation to the historical data used as a base for this study.

On the other hand, the hepatitis C market has been sharply increasing, the market is historically almost 100% under exclusivity (2006-2016). The strategies adopted to try to remove IPR barriers[viii] had not yet fully resulted in changes in the market as of December 2016, resulting in a market in which the negative impact of IPR on public expenditures and local production can be measured in full.

For these reasons we consider the ARV market and the hepatitis C market to be key case studies to simulate and illustrate the implications on public expenditures and

[viii] There have been patent oppositions filed in Brazil against patent applications related to sofosbuvir and daclatasvir, by Farmanguinhos/Fiocruz and GTPI/Rebrip – Intellectual Property Working of the Brazilian Network for the Integration of the Peoples, a group of Brazilian civil society organizations. Final decision from the Brazilian patent office is still pending in both cases.

sales by domestic producers with the adoption of TRIPS-plus provisions proposed by the EU in the FTA negotiations with Mercosur.

***Data and information sources***

The data related to prices, volume of purchases and suppliers of ARV medicines in the period of 2008 to 2015 used in the application of the IPRIA Model was supplied by the Brazilian Ministry of Health (MoH) through the Access to Information Act[ix]. The data related to hepatitis C medicines was also obtained from the MoH for the year 2016 and for the period of 2006-2015 we used data available in a previous study recently published by one the authors[34].

Data related to regulatory market authorization was obtained at the official website of Anvisa (*Agência Nacional de Vigilância Sanitária*)[x]. Data related to patents was obtained at the official website of the Brazilian Patent Office - INPI (*Instituto Nacional de Propriedade Industrial*)[xi].

***Base and Alternative scenarios***

The IPRIA Model is based on the "scenario method". Information on the medicines market selected is obtained by comparing alternative scenarios to a base scenario. The impact is the result of the difference between a basic scenario, which, in the prospective simulation, describes the current situation and its possible evolution if there are no changes in IP regulation, and different alternative scenarios that describe possible evolutions according to different changes in IPR.

The data used for the base scenario is the state of the market in the first year of the simulation (2015 for ARV and 2016 for hepatitis C). The variables that characterize the initial year of the simulation are the same in the baseline scenario and in all alternative scenarios. These variables are based on actual data as far as they are available. If not

[ix] We also looked at two other sources: the Public Transparency Portal (Portal da Transparência), which gathers information on public spending by all branches of the Federal Administration; and the Health Prices Bank (Banco de preços em saúde), an online repository of public purchases of medicines. These two were abandoned in favour of the former because in the data provided by the MoH the information was more complete, especially since the previously mentioned databases don't include information of purchases from public laboratories.

[x] www.anvisa.gov.br

[xi] www.inpi.gov.br

so, they must be estimated outside the model by extrapolating previous figures and trends or by expert opinion. In order to simulate posterior years of the baseline and of the alternative scenarios it is necessary to populate the model with the parameters requested by it. The values of these parameters can be based on an extrapolation of past trends or on justified assumptions on the future evolution of the market.

There were two main outcomes considered for this study: (i) changes in public expenditures; and (ii) changes in the sales of domestic producers. The latest was only calculated for the ARV market, as the sales of domestic producers (only ribavirin) in the hepatitis C market in Brazil are considered residual.

The simulation of each scenario is based on a series of parameters (Chart 2). These are: (i) fixed parameters, which are the same for every scenario; (ii) scenario-specific parameters, which describe the projected changes in each scenario; and (iii) annual input data, which give the simulations substance in order to produce predictions based on actual market behaviour. Therefore, the Model uses the historical market parameters to simulate different future scenarios keeping the same market parameters to simulate the impact of the changes in the IP regulations.

**Chart 2 - Description of the parameters**

| Fixed parameters | Description |
|---|---|
| YI | The initial year of simulation. |
| YL | The final year of simulation. |
| TAPto | Number of medicines on the first year of the simulation. |
| MVto | The value of the market on the first year of the simulation. |
| A | Annual growth rate of the market. |
| D | Discount rate. |
| kde | Market share of domestic industry in market under exclusivity. |
| kdc | Market share of domestic industry in market under competition. |
| **Scenario-Specific Parameters** | **Description** |
| YP | Year of the introduction of product patents. |
| YDP | Year of the introduction of data exclusivity. |
| PD | The term of a patent in years. |
| DT | Average time from patent application and market registration. |
| PDE | Extension of patent term due to marketing approval or patent examination delay. |
| pPDE | The proportion of medicines obtaining an extension of patent term due to delay in market approval. |
| TTC | The time lag between the expiry of a patent of an originator product and entry of generics. |
| DE | The period of data exclusivity. |
| RPec | The price differential between the average price of a drug under market exclusivity and that under competition. |

| e | Price-elasticity of demand. |
|---|---|
| **Annual Input Data** | **Description** |
| Ali | The number of new medicines entering the market in a particular year. |
| AOI | The number of medicines exiting the market in a given year. |
| AIPPi | The number of medicines that enter the market in a particular year with (product) patent protection. |

Source: Rovira (2009)

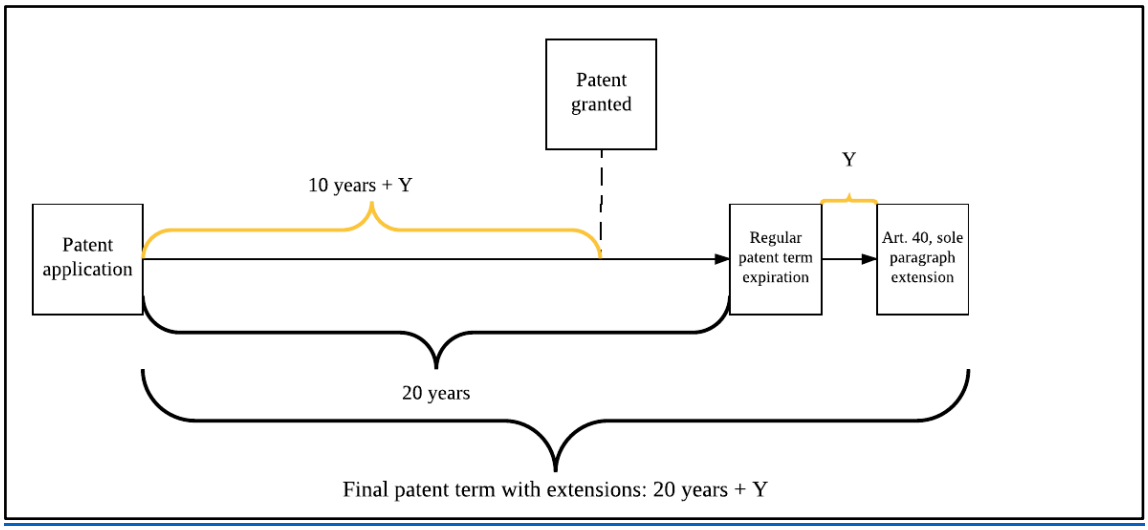
### *TRIPS-plus provisions considered for the simulation of the scenarios*

*Alternative scenario 1 - Patent term extension due to delay on patent examination*

Brazilian patent law allows for patent term extension when a patent application takes more than 10 years to be granted. The extension will be of Y years, where Y is the number of years that surpass 10 years after the date of application in the country (Figure 1). That is, a patent application that takes 11 years to be granted will have a total patent term of 21 years counting from the application date, instead of 20[xii]. This period begins from the application date, that is, it is retroactive. **In the model, this extension is incorporated into the base scenario** and an alternative prospective scenario without it is simulated in order to estimate its impact.

[xii] It should be noted that during the time in which the patent application is pending analysis, there is a de facto monopoly due to the risk of entering the market and facing litigation or the payment of damages in case the patent is granted. This will be further developed in another study under the AccessIBSA Project.

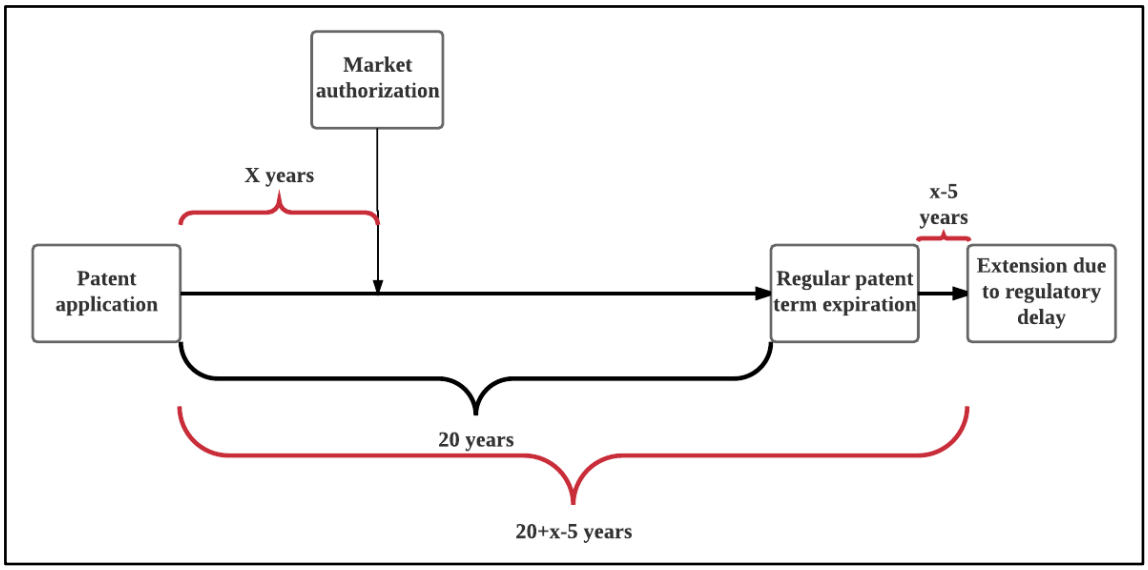
**Figure 1 – Patent term extension due to delay on patent examination under article 40, sole paragraph of the Brazilian patent law**




*Alternative scenario 2 - Patent term extension due to delay in obtaining market authorization*

The EU FTA proposal establishes the adoption of a new patent term extension not yet adopted in Brazil: an extension to patent term due to the time lag between patent application and market approval (Figure 2). This would be calculated as the time between filing a patent and obtaining market approval minus 5 years.

**Figure 2 - Patent term extension due to delay in obtaining market approval as proposed by the EU on the negotiations of the Mercosur-EU FTA**




For the purpose of this study, we estimated the average time frame between the filling of the oldest patent application for each medicine (either granted or pending) in the country and the date of obtaining the first sanitary registration, and reduced the 5 years mentioned in the proposal (Chart 3). Granted patents and pending applications were considered assuming the chance of those pending of being granted and the *de facto* monopoly created by the legal uncertainty.

**Chart 3 - Estimates of patent term extension due to delay in patent examination (Brazilian law) or in the delay to obtain market authorization (EU proposal for the FTA)**

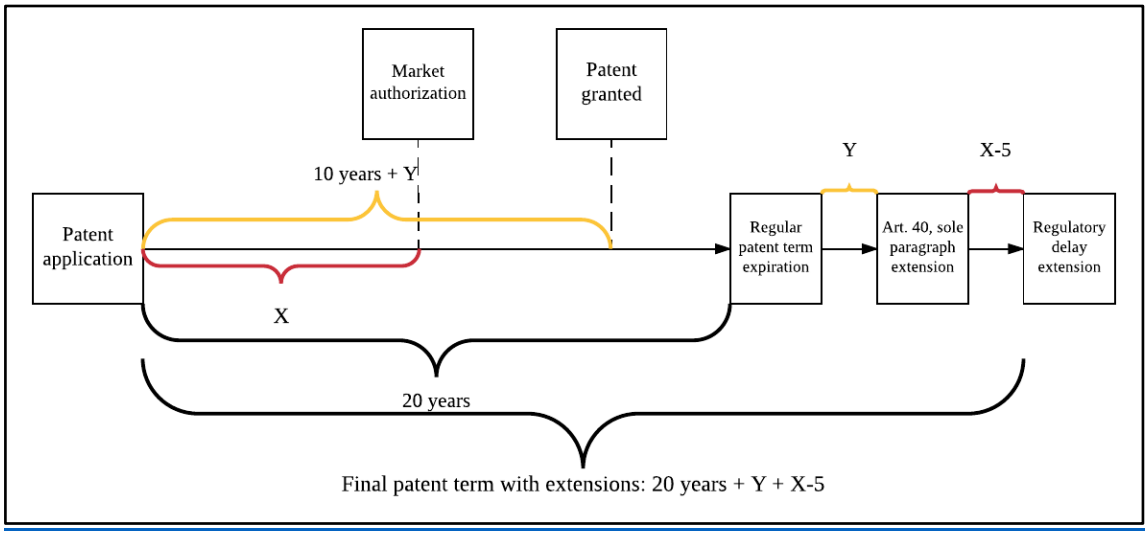
| | ARV | | Hepatitis C | |
|---|---|---|---|---|
| | Years | Proportion of patent applications in which the provision was applied | Years | Proportion of patent applications in which the provision was applied |
| Average patent term extension due delay in patent examination* | 5.61 (rounded to 6) | 0.27 | 4.3 (rounded to 4) | 0.43 |
| Average patent term extension due to delay in regulatory market authorization | 4.52 (rounded to 5) | 0.45 | 5.2 (rounded to 5) | 0.71 |

* The average was calculated based in real terms for patents already granted and for patents still pending we considered as granted date the last day of December 2015 for ARV and of 2016 for hepatitis C medicines.

Considering the base scenario takes into consideration the current Brazilian patent law, including the TRIPS-plus provision that provides for patent term extension due to delay in patent examination, it was estimated the cumulative effect of patent extension by both delay in patent examination and regulatory market authorization (Figure 3).

The wording provided by the EU text suggests this additional protection period will begin after the lawful patent term – or, to be more precise, it would be added to the final patent term even if it had already been extended by other provisions, such as the one in article 40 of the Brazilian law[xiii].

**Figure 3 - Patent term extension based on the cumulative effect of extension due to delay in patent examination and delay in market authorization**

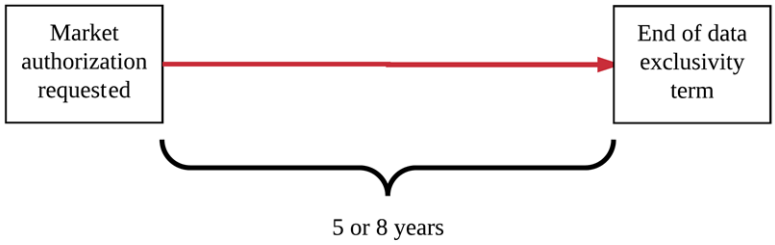



*Data exclusivity*

Data exclusivity is another of the TRIPS-plus measures contained in the EU proposal. This would grant exclusivity over the test data required for sanitary registration of medicines to the first registering company (Figure 4). The period is not defined in the proposal, but in other agreements the EU has set it to a minimum of 5 years and 8 years. Thus, we have simulated both cases - 5 and 8 years - as the period of exclusivity for the alternative scenarios where data exclusivity would be implemented in Brazil.

[xiii] This is not unprecedented: e.g., U.S. law states that the "patent term extension that may be available under 35 U.S.C. 156 for premarket regulatory review is separate from and will be added to any extension that may be available under former and current 35 U.S.C. 154".

**Figure 4 – Data exclusivity for a period of 5 or 8 years**




***Description of the parameters adopted***

*ARV market*

The evolution of the ARV pharmaceutical market in Brazil was based on data collected from the Ministry of Health based on expenditures from 2008 to 2015. This aggregate annual data was adjusted to the inflation of 2015 by adopting the IPCA - Índice Nacional de Preços ao Consumidor index (Chart 4).

The Model considers the parameters of historical data to simulate prospective scenarios based on the market behaviour and not on the specific information of individual drugs available in the first year of the simulation. That is, the Model considers the inclusion and exclusion of new products, the proportion of products under exclusivity or on competition, the status in which new products enter into the market and so on in order to simulate the behaviour of the market in future years.

**Chart 4 - Estimated public expenditure on ARV and the number of people under treatment. Brazil, 2008 to 2015.**

| Year | Total expenditures in current values (unadjusted) (BRL) A1 | Total expenditures adjusted to the inflation* (BRL) A2 | Number of people on ARV treatment B | Variation in number of people on ARV treatment | Expenditure per person on treatment (unadjusted) (BRL) (A1/B) | Expenditure per person on treatment (adjusted) (BRL) (A2/B) |
|---|---|---|---|---|---|---|
| 2008 | 593,478,608.93 | 921,757,635.10 | 190,506 | - | 3,115.47 | 4,838.47 |
| 2009 | 671,304,484.71 | 999,551,733.50 | 231,146 | 21.33% | 2,904.24 | 4,324.33 |
| 2010 | 830,297,809.46 | 1,167,300,448.20 | 257,000 | 11.18% | 3,230.73 | 4,542.02 |

| Year | Total expenditures in current values (unadjusted) (BRL) A1 | Total expenditures adjusted to the inflation* (BRL) A2 | Number of people on ARV treatment B | Variation in number of people on ARV treatment | Expenditure per person on treatment (unadjusted) (BRL) (A1/B) | Expenditure per person on treatment (adjusted) (BRL) (A2/B) |
|---|---|---|---|---|---|---|
| 2011 | 795,000,612.47 | 1,049,461,753.00 | 284,390 | 10.65% | 2,795.45 | 3,690.22 |
| 2012 | 734,868,139.04 | 916,555,440.60 | 313,175 | 10.12% | 2,346.50 | 2,926.65 |
| 2013 | 728,767,666.39 | 858,225,568.40 | 354,519 | 13.20% | 2,055.65 | 2,420.81 |
| 2014 | 870,806,581.05 | 963,721,643.20 | 403,970 | 13.94% | 2,155.62 | 2,385.62 |
| 2015 | 1,119,149,617.60 | 1,119,149,617.60 | 454,615 | 12.53% | 2,461.75 | 2,461.75 |
| **Annual rate of market increase** | 9.5% (rounded to 9%) | 2.8% (rounded to 3%) | | | | |

* Values adjusted to inflation according to IPCA 2015.
Source: Ministry of Health, Brazil. Access to information law.

From these values, we calculated the average growth rate of the market. This is expressed in Brazilian Reais (BRL). A Compound Annual Growth Rate (CAGR) formula was adopted and estimated considering the evolution of the market adjusted and not adjusted by the inflation, as follows: (a) CAGR (2008, 2015) = 2.8% (adjusted); CAGR (2008, 2015) = 9.5% (not adjusted).

The average of inclusions and exclusions of ARV in the market was based on historical data of ARV, as shown in Figure 5. The ARV market in 2015 was composed of 22 APIs that were purchased by the MoH, including a drug that had been excluded from treatment guidelines in the previous year, considering that this would more adequately reflect the market scenario. It is important to note that fixed-dose combinations (FDC) were considered as one API, as they behave in the market as a single API. First market registrations were obtained in the dates described in Figure 6.

**Figure 5 - Inclusions and exclusions of ARV on SUS, 1991 - 2015**

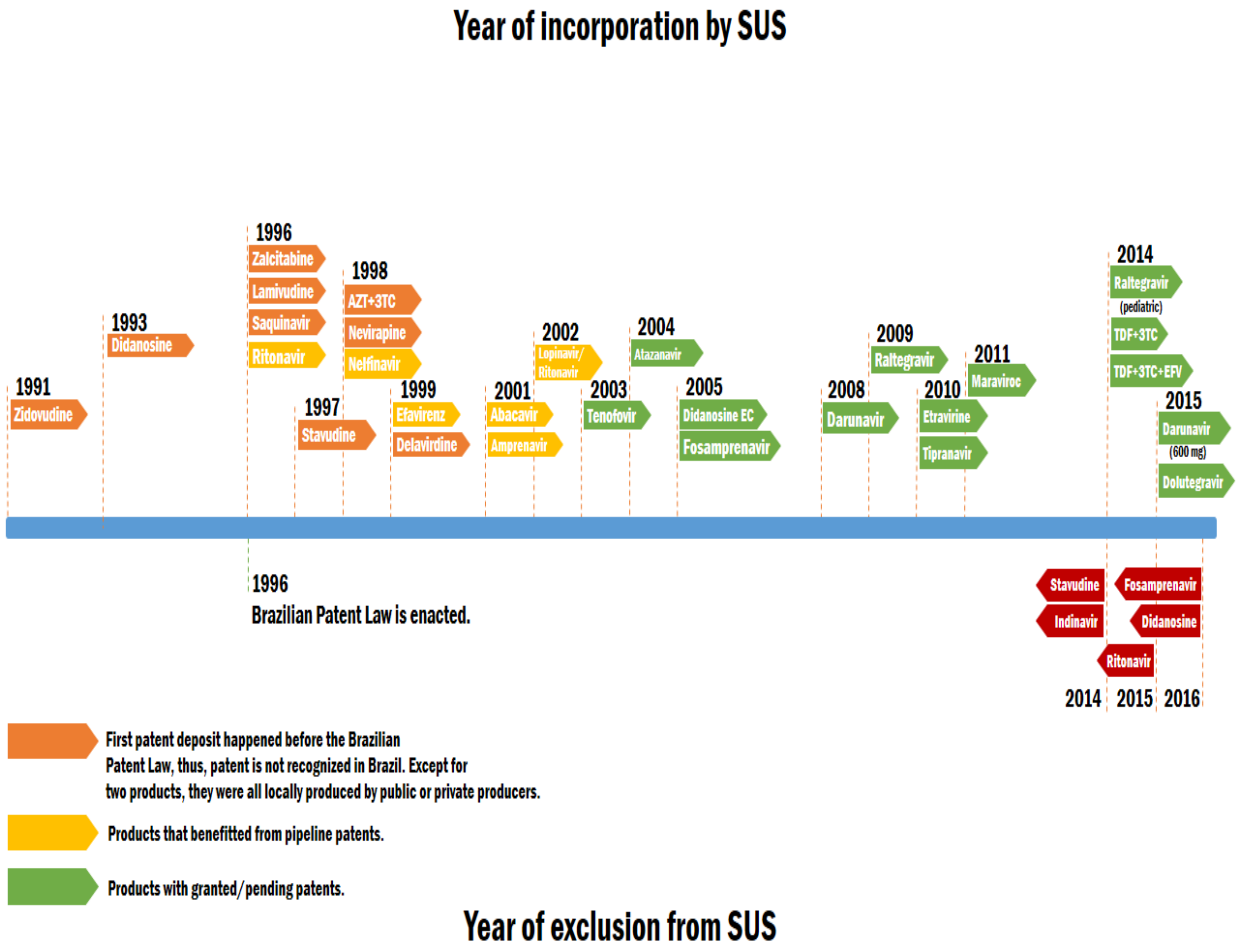
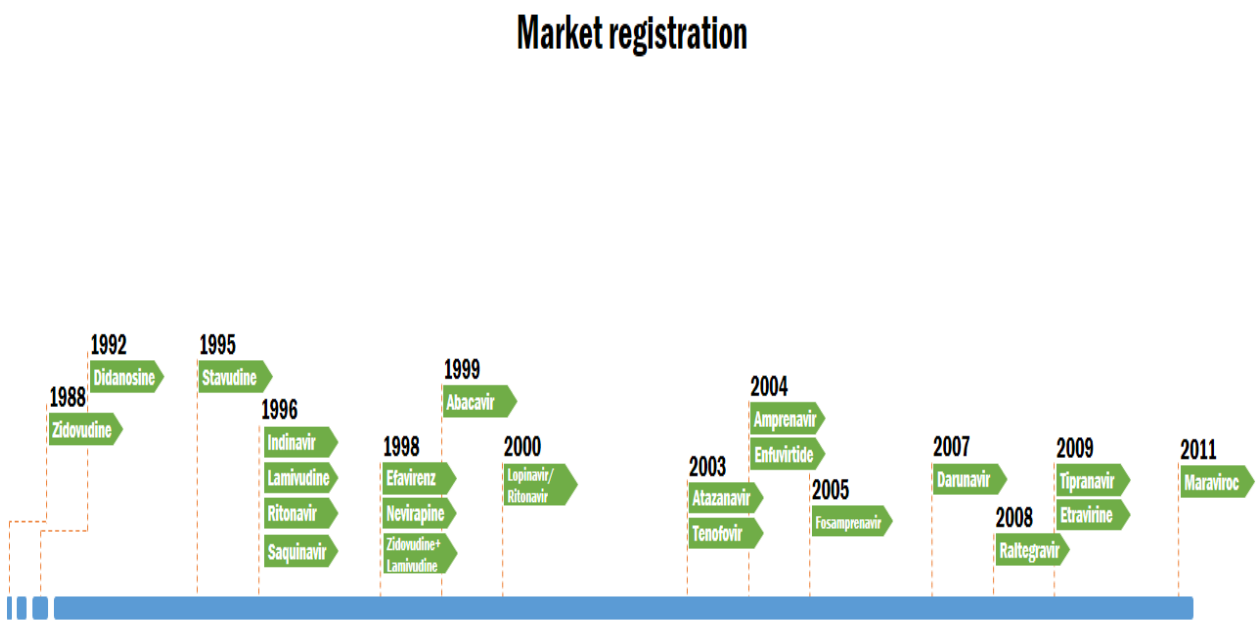


**Figure 6 – Dates of market approval of ARV in Brazil, 1988-2015**




*The complexity of patent situation and market exclusivity in the Brazilian pharmaceutical market*

The ARV market is also illustrative of a complex configuration in the Brazilian pharmaceutical market. According to several studies on patent landscape of ARV in Brazil [31-33], for all ARV adopted by the national therapeutic guidelines there are related patent applications. However, this does not necessarily mean that all ARV are under exclusivity in the country.

We observe at least four main situations:

a) ARV adopted by SUS between 1991 and 1998 that was subjected to domestic production. This allows the interpretation that the industrial property law 9.279, enacted in 1996, did not apply to the initial patent applications related to those medicines, leading to a situation of competition even if late after there were other secondary patent applications related to the medicine;
b) ARV in which the first patent in the country was granted through the pipeline mechanism, as mentioned before, a TRIPS-plus provision in the Brazilian law which allowed for retroactive patent protection in the country through the revalidation of patents granted abroad, were generally under exclusivity;

c) ARV in which patents granted or pending create a monopoly situation for the product. In the case of products with pending patent applications this can be the result of competitors not willing to take the risk of entering the Brazilian market or public purchasers interpreting that the product is under monopoly[xiv];
d) Fixed-dose-combinations in which active pharmaceutical ingredients (API) are in public domain, but there are pending patent applications for the combination. The MoH is purchasing the generic version of those products.

ARV exclusivity situation was assessed on the basis of above-mentioned criteria as well as on the trend in public procurement from one or more producers (Chart 5).

**Chart 5 - Patent status of ARV and assessment of exclusivity situation in 2015 in Brazil**

| Product | Number of patent applications in Brazil | Patent status in 2015 | Market situation in 2015 | Justification |
|---|---|---|---|---|
| Abacavir | 17 | 3 granted (1 expired); 5 pending; 2 rejected; 7 filed before analysis | Exclusive | 3 granted patents and 4 pending applications. Public procurements supplied by the multinational company (GSK), except in 2012 (Aurobindo) |
| Amprenavir | 1 | Expired | Not available | Not applied |
| Atazanavir | 7 | 1 granted; 2 pending; 2 rejected; 2 filed. | Non-Exclusive | Since 2015, there is a generic version available from Farmanguinhos (national public producer) developed under a technology transfer and voluntary license with BMS. |
| Darunavir | 15 | 1 granted (currently abandoned); 8 pending; 2 rejected; 4 filed before analysis | Exclusive | 1 granted patent (currently abandoned); 8 pending application. Public procurements supplied by the multinational company (Janssen-Cilag) |
| Didanosine EC | 2 | 1 granted; 1 rejected | Exclusive | 1 patent granted related to the enteric-coated formulation. Public procurement supplied the multinational company (BMS) |
| Efavirenz | 21 | 3 granted (1 expired); 3 pending; 3 rejected; 12 filed | Non-exclusive | Product under a compulsory license since 2007. Public procurements supplied by Indian generic companies and/or |

[xiv] This issue is currently under development in another study of the AccessIBSA project and results are expected to be released by the end of 2017.

| Product | Number of patent applications in Brazil | Patent status in 2015 | Market situation in 2015 | Justification |
|---|---|---|---|---|
| | | | | Brazilian public manufacturers. |
| Enfuvirtide | 8 | 1 pending; 2 rejected; 5 filed before analysis | Exclusive | Although most applications are rejected or filed, there is one pending application. All public procurements were supplied by the multinational company (Roche) |
| Stavudine | 6 | Not applied (locally produced since 1990) | Not available | Locally produced since 1990 decade |
| Etravirine | 8 | 1 granted; 6 pending; 1 filed before analysis | Exclusive | 1 granted patent; 6 pending applications. Public procurements supplied by the multinational company (Janssen-Cilag) |
| Fosamprenavir | 13 | 2 granted (1 expired); 1 pending; 5 rejected; 5 filed before analysis | Exclusive | 1 granted patent; 1 pending application. Public procurements supplied by the multinational company (GSK) |
| Indinavir | 13 | Not applied (locally produced since 1990) | Non-exclusive | Locally produced since 1990 decade |
| Lamivudine (3TC) | 27 | Not applied (locally produced since 1990) | Non-exclusive | Locally produced since 1990 decade |
| Lopinavir / ritonavir | 12 | 1 granted; 7 pending; 3 rejected; 1 filed before analysis | Exclusive | 1 granted patent; 7 pending applications. Public procurements supplied by the multinational company (Abbott/Abbvie) |
| Maraviroc | 7 | 2 pending; 1 rejected; 4 filed before analysis | Exclusive | 2 pending applications. Public procurements supplied by the multinational company (GSK) |
| Nevirapine | 4 | Not applied (locally produced since 1990) | Non-exclusive | Locally produced since 1990 decade |
| Raltegravir | 5 | 2 pending; 3 filed before analysis | Exclusive | 2 pending applications. Public procurements supplied by the multinational company (MSD) |
| Ritonavir | 22 | Not applied (locally produced) | Non-exclusive | Locally produced |
| Saquinavir | 14 | Not applied (locally produced since 1990) | Non-exclusive | Locally produced since 1990 decade |
| Tenofovir | 16 | 3 rejected; 11 pending; 2 filed | Non-exclusive | Main patent rejected. Public procurements supplied by public manufacturers since 2011 |
| TDF+3TC | Not found | Not applied. | Non-exclusive | Public procurements supplied by public manufacturer |

| Product | Number of patent applications in Brazil | Patent status in 2015 | Market situation in 2015 | Justification |
|---|---|---|---|---|
| | | | | (Farmanguinhos/Fiocruz) |
| TDF+3TC+EFV | Not found | Not applied. | Non-exclusive | Public procurements supplied by PAHO Strategic Fund |
| Tipranavir | 8 | 1 granted; 2 pending; 2 rejected; 3 filed before analysis | Exclusive | 1 granted patent; 2 pending applications. Public procurements supplied by the multinational company (Boehringer) |
| Zidovudine (AZT) | 1 | Not applied (locally produced since 1990) | Non-exclusive | Locally produced since 1990 decade |
| AZT+3TC | Not found | Not applied (locally produced since 1990). | Non-exclusive | Locally produced since 1990 decade |

To estimate the average of price reduction (RPec) after generics enter the market, we identified three ARV which had generics first registered in Brazil in the period from 2008 to 2015. The table below shows the difference between the price of the branded-version in the year immediately before the generic version was purchased and the price of the generic in the first year it entered the market (

Chart 6). However, as atazanavir is being produced under a voluntary license of the patent in a context of a public-private partnership for technology transfer from BMS to Farmanguinhos, it cannot be considered under generic competition in the same way as the cases for efavirenz and tenofovir. Therefore, to estimate the average of price reduction after generics enter the market we considered only the case of efavirenz and of tenofovir. This resulted in an average of price reduction of 55.6% (

Chart 6).

It should be noted that the generic production of tenofovir was made possible in a context in which the patent application was denied by the Brazilian patent office in 2009 following patent oppositions filed by generic producers and civil society organizations. The generic production of efavirenz was possible under a compulsory license issued in 2007, which is by definition non-exclusive. Therefore, in both cases the generic version could be introduced to the Brazilian market before the initial expected patent expiration due to the adoption of strategies to remove the patent barrier.

**Chart 6 - Estimated price reduction of selected ARV**

| Product | Situation | Originator price (year)* | Generic price (year)* | Reduction (%) |
|---|---|---|---|---|
| Efavirenz 600 mg | Compulsory license issued in 2007 | 6.43 (2006) | 1.47** (India, 2007)/2.1 (Brazil, 2009) | 77%/67% |
| Tenofovir 300 mg | Patent application rejected by the Patent Office in 2009. First generic procurement in 2011 | 9.45 (2009) | 5.31 (2011) | 44% |
| Atazanavir 300mg | Voluntary license and technology transfer to a public manufacturer (Farmanguinhos) in 2014. | 6.57 (2013) | 6.04 (2014) | 8% |
| Average reduction (without atazanavir) | | | | 55.6% (rounded to 56% |

* All prices were adjusted to the inflation according to IPCA 2015

** There were purchases from both Ranabaxy and Aurobindo, same volume. Indicated price was the average of each: R$ 1.46 and R$ 1.47.

Elasticity was set to zero (0) because the government has a duty to provide medicines as a component of the constitutional right to health and there is a specific law on the obligation to provide treatment for HIV (Law 9,316/96), so it is assumed amounts purchased would not be greatly reduced in the face of price increases.

The time horizon for this prospective simulation is 35 years, from 2015 to 2050, allowing enough time for the projected policy changes to produce effects.

To calculate the average time between patent expiry and generic entry in the market, we looked at the generics registrations first obtained during the time frame adopted by the study. As the registration was made before patent expiry, so the period between one and the other was set to 0 considering that generics would have been able to enter the market as soon as the patent expired (Chart 7). It should also be

noted that Brazilian IP law has adopted the Bolar exception[xv], which allows generic drug manufacturers to prepare all necessary documents for regulatory approval during the validity of the patent, allowing the generic to be put in market just after the patent expiries or the exclusivity is removed. Some of the cases were also possible because the patents were licensed compulsorily (efavirenz) and voluntarily (atazanavir).

**Chart 7 - First generic registrations for selected API**

| Active ingredient | Patent expiry | First generic registration |
|---|---|---|
| Atazanavir* | 22/04/17 | 2014 |
| Efavirenz** | 09/04/17 | 2009 |
| Lopinavir+Ritonavir | 30/04/17 | 2016 |

*The generic entry was made possible before the patent expiration because there was a voluntary license granted by BMS to Farmanguinhos/Fiocruz in the context of a technology transfer agreement.
**The generic entry was made possible before the patent expiration because there was a compulsory license issued in 2007.

The average time between patent application and regulatory approval (DT) was estimated based on the data of the first market approval in Brazil and the oldest patent application in the country (Chart 8).

**Chart 8 - Time between patent application and market registration (years)**

| Product | Brazilian patent number | Patent filing date* | Market registration date | Time lag: patent filing / market registration (years) |
|---|---|---|---|---|
| Abacavir | PI9506667-5 | 02/03/1995 | 16/03/1999 | 4.041096 |
| Atazanavir | PI9701877-5 | 22/04/1997 | 18/09/2003 | 6.410959 |
| Darunavir | PI9607625-9 | 03/07/1996 | 21/05/2007 | 10.88767 |
| Didanosine EC | PI9106503-8 | 05/08/1991 | 11/06/1992 | 0.852055 |
| Efavirenz | PI9608839-7 | 21/05/1996 | 03/11/1998 | 2.454795 |
| Enfuvirtide | PI9609152-5 | 06/06/1996 | 31/05/2004 | 7.989041 |
| Etravirine | PI9915176-6 | 11/04/1999 | 02/02/2009 | 9.821918 |
| Fosamprenavir | PI9608032-9 | 18/04/1996 | 26/12/2005 | 9.69589 |
| Indinavir | PI9406503-9 | 24/03/1994 | 01/04/1996 | 2.024658 |
| Lamivudine | PI9507499-6 | 21/04/1995 | 13/05/1996 | 1.063014 |
| Lopinavir/ritonavir | PP1100397-9 | 30/04/1997 | 09/10/2000 | 3.446575 |
| Maraviroc | PI9916585-6 | 12/01/1999 | 07/02/2011 | 12.07945 |
| Raltegravir | PI0011939-3 | 22/06/2000 | 28/01/2008 | 7.605479 |
| Saquinavir | PI9006264-7 | 12/10/1990 | 26/02/1996 | 5.378082 |

[xv] Article 43, VII Law 9279/96.

| Product | Brazilian patent number | Patent filing date* | Market registration date | Time lag: patent filing / market registration (years) |
|---|---|---|---|---|
| Tenofovir | PI9205661-0 | 20/02/1992 | 07/06/2003 | 11.30137 |
| Tipranavir | PI9507615-8 | 05/04/1995 | 20/04/2009 | 14.05205 |
| **AVERAGE** | | | | 6.819006375 |

* It was considered the oldest patent application in Brazil for each product

The average of inclusions (Ali) and exclusions (AOi) was estimated based on the number of inclusions (27) and exclusions (7) in 24 years (1991-2015) as in Chart 9. For the purpose of the baseline data, we considered this average for the period of 2017-2050. For 2016, we considered the inclusion of one ARV (dolutegravir) and exclusion of two ARV (fosamprenavir and DDi EC). However, there were procurements of excluded ARV in the following years. So, this figure was used to estimate the variables Ali and AOi.

**Chart 9 - Average of inclusions and exclusions of ARV**

| Data | Number | Average of inclusion/exclusion per year |
|---|---|---|
| Number of inclusions of ARV from 1991-2015 | 27 | 1.1250 |
| Number of exclusions of ARV 1991-2015 | 7 | 0.29166) |

In order to estimate the number of API losing patent protection, we considered the oldest granted patent or pending patent application, as shown in Chart 10.

**Chart 10 - Estimate of API losing patent protection**

| Products | Patent number | Estimated expiring year |
|---|---|---|
| Abacavir | PI9506667-5 | 2015 |
| Atazanavir | PI9701877-5 | 2017 |
| Darunavir | PI9607625-9 | 2013 (not included) |
| Didanosine EC | PI9815861-9 | 2018 |
| Enfuvritide | PI0312889-0 | 2017 (withdrawn)* |
| Etravirine | PI9915552-4 | 2019 |
| Fosamprenavir | PI9708238-4 | 2017 |
| Lopinavir/ritonavir | PI1100397-9 | 2017 |
| Maraviroque | PI9917007-8 | 2026 |
| Raltegravir | PI0213522-1 | 2027 |
| Tipranavir | PI9507615-8 | 2015 |

*As we assumed pending applications created an exclusivity situation, we also considered the year of withdrawn as rejected

All these parameters are summarized in the table below, referring to the various scenarios calculated in the prospective simulation (Chart 11).

**Chart 11 - Prospective simulation, parameters used for ARV market**

| Fixed param. | Value (base scenario) | (w/o art. 40 ext.) | (data exclus.) | (reg. delay comp.) | (base + data exclusivity + regulatory delay) |
|---|---|---|---|---|---|
| YI | 2015 | 2015 | 2015 | 2015 | 2015 |
| YL | 2050 | 2050 | 2050 | 2050 | 2050 |
| TAPto | 22 | 22 | 22 | 22 | 22 |
| MVto | R$ 1.119.149.617 .60 | R$ 1,119,149,617 .60 | R$ 1,119,149,617 .60 | R$ 1,119,149,617 .60 | R$ 1,119,149,617 .60 |
| α | 0.03 | 0.03 | 0.03 | 0.03 | 0.03 |
| d | 0.03 | 0.03 | 0.03 | 0.03 | 0.03 |
| $k_{de}$ | 0 | 0 | 0 | 0 | 0 |
| $k_{dc}$ | 0.84 | 0.84 | 0.84 | 0.84 | 0.84 |
| **Scenario-Specific** | **Value (base scenario)** | **(w/o art. 40 ext.)** | **(data exclus.)** | **(reg. delay comp.)** | **(all three cases)** |
| YP[xvi] | 1997 | 1997 | 1997 | 1997 | 1997 |
| YDP[xvii] | 2050 | 2050 | 2015 | 2050 | 2015 |
| PD | 20 | 20 | 20 | 20 | 20 |
| DT[xviii] | 7 | 7 | 7 | 7 | 7 |
| PDE | 6 | 0 | 6 | 11 | 11 |
| pPDE | 0,3 | 0 | 0,3 | 0,3 | 0,3 |
| TTC | 0 | 0 | 0 | 0 | 0 |
| DE | 0 | 0 | 5 / 8 | 0 | 5 / 8 |
| RPec | 2.3 | 2.3 | 2.3 | 2.3 | 2.3 |
| e[xix] | 0 | 0 | 0 | 0 | 0 |
| **Annual Input** | **Value (base scenario)** | **(w/o art. 40 ext.)** | **(data exclus.)** | **(reg. delay comp.)** | **(all three cases)** |
| Ali[xx] | 1.125 | 1.125 | 1.125 | 1.125 | 1.125 |
| AOI | 0.29 | 0.29 | 0.29 | 0.29 | 0.29 |
| AIPPi | 0.9 | 0.9 | 0.9 | 0.9 | 0.9 |

Domestic and foreign industry values were estimated based on the supplier for each product in 2015 (Chart 12 and Chart 13). There were 11 products under exclusivity and

[xvi] The current patent law, which establishes product patents for pharmaceuticals, was enacted in 1996 and went into effect in 1997. It should be noted that the law allowed for the granting of pharmaceutical patents retrospectively, through the mechanism known as "pipeline". The model takes into consideration patents in force before the base year.

[xvii] Exclusivity of test data doesn't exist under the current Brazilian law for health products of human use. Thus, the year for its introduction was initially set to the final simulation year, so it wouldn't affect the final result. This is changed in alternative scenarios to simulate the effect of adopting data exclusivity.

[xviii] This data was calculated case by case for the 24 ARV based on patent and sanitary registration information, and then an average was calculated.

[xix] Considering that provisionof antiretroviral is mandated by law, we expect demand not to vary with price hikes, thus it is inelastic, that is, its price-elasticity equals zero.

[xx] This number was estimated based on the average of inclusions in 24 years (27 inclusions). The data on entries and exits were obtained from public therapeutic protocols.

11 without exclusivity. In markets without exclusivity, there were 6 national producers (including public and private), which amounted for approximately 84% of the market without exclusivity (Chart 13).

**Chart 12- Market share of foreign and national companies in 2015**

| Product | Market situation in 2015 | Market-share in 2015 (in monetary values) | Supplier in 2015 |
|---|---|---|---|
| Abacavir | Exclusive | 0.26% | GSK |
| Atazanavir | Exclusive | 12.70% | Farmanguinhos/Fiocruz (ongoing technology transfer with BMS) |
| Darunavir | Exclusive | 7.14% | Janssen-Cilag |
| Didanosine EC | Exclusive | 0.30% | BMS |
| Efavirenz (EFV) | Non-exclusive | 0.01% | Aurobindo |
| | | 6.73% | Farmanguinhos/Fiocruz |
| | | 0.04% | MSD |
| Enfuvirtide | Exclusive | 0.81% | Roche |
| Stavudine | Non-exclusive | 0.02% | Cristália |
| Etravirine | Exclusive | 1.66% | Janssen-Cilag |
| Fosamprenavir | Exclusive | 1.43% | GSK |
| Lamivudine (3TC) | Non-exclusive | 1.42% | Lafepe, Iquego, Furp |
| | | 0.10% | Aurobindo |
| Lopinavir/ ritonavir | Exclusive | 13.90% | Abbvie |
| Maraviroc | Exclusive | 0.66% | GSK |
| Nevirapine | Non-exclusive | 0.64% | Farmanguinhos/Fiocruz |
| | | 0.01% | Aurobindo |
| Raltegravir | Exclusive | 8.74% | MSD |
| Ritonavir | Non-exclusive | 4.35% | Abbvie |
| Saquinavir | Non-exclusive | 0.10% | Cristália |
| Tenofovir (TDF) | Non-exclusive | 3.08% | Funed |
| | | 5.13% | Lafepe |
| TDF+3TC | Non-exclusive | 11.53% | Farmanguinhos/Fiocruz |
| TDF+3TC+EFV | Non-exclusive | 5.90% | PAHO |
| Tipranavir | Exclusive | 0.14% | Boehringer |
| Zidovudine (AZT) | Non-exclusive | 0.10% | Farmanguinhos/Fiocruz |
| | | 0.01% | Cristália |
| | | 0.05% | Lafepe |
| AZT+3TC | Non-exclusive | 13.25% | Lafepe, Iquego, Furp, Farmanguinhos/Fiocruz |

**Chart 13 - Market share of ARV according to the exclusivity situation in 2015**

| | |
|---|---|
| **Market share of API under exclusive market** | 35.04% |
| **Market share of API on non-exclusive market** | 65.17% |
| **Market share of domestic industry under exclusive market** | 0 |
| **Market share of domestic industry under non-exclusive market** | 84% |

*Hepatitis C market*

Since 1980, the Brazilian government has implemented policies related to viral hepatitis. Different initiatives were incorporated in the response, such as: compulsory notification; prevention; diagnosis; and treatment. In relation to hepatitis C, it is estimated that there are 1.5 million of people infected with the virus (HCV) in Brazil. In 2000, it was published the first therapeutic guideline. Initially, treatment involved conventional alfainterferon 2a and 2b monotherapy; then, peginterferon 2a or 2b plus ribavirin regimen (since 2000)[34].

In 2012, the new direct-acting antiviral drugs (DAA) – boceprevir and telaprevir – were included as part of the therapeutic regimen. In 2015, three additional DAA were incorporated – sofosbuvir, daclatasvir and simeprevir. The adoption of DAA in the treatment has been a landmark in terms of the increase of the Ministry of Health expenditures, as shown in Chart 14, highlighting real concerns related to the sustainability of the access policy.

The period considered for this is study is related to the beginning of centralization of the purchases of hepatitis C medicines by the Ministry of Health in 2006 until 2016.

The hepatitis C market has been sensitive to adoption of newer technologies. Since 2006 and 2007, the increase in expenditure was reflected by the procurement of peginterferon 2a and 2b and also by the increase in volume. Due to price reductions of those technologies between 2007 and 2011, it was possible to have a decrease in expenditures followed by an increase in volume purchased (Annex 1). The adoption of DAA had a significant increase in expenditures, as shown from 2012 to 2016. In 2015, the procurement of only four DAA achieved BRL 1 billion. Considering only sofosbuvir,

the volume purchased in 2015 and 2016 was equivalent, respectively, to 31,956 and 35,056 treatments[xxi].

The evolution of the hepatitis C pharmaceutical market in Brazil was based on data collected from the Ministry of Health based on expenditures from 2006 to 2016. From the period 2006 to 2014, this did not include data on procurement direct from the public manufacturer on ribavirin. However, according to Chaves et al. (2017), the weight of ribavirin in the cost of the treatment is residual compared to the weight of other medicines such as peginterferon and later DAAs in therapeutic regimens. For 2015 and 2016, as the data was collected directly from Access to Information Law, there was no procurement of ribavirin from any supplier.

This aggregate annual data was adjusted to the inflation of 2016 by adopting the IPCA index (Chart 14). From these values, we calculated the average growth rate of the market. A Compound Annual Growth Rate (CAGR) formula was adopted and estimated considering the evolution of the market adjusted by the inflation, as follows: (a) CAGR (2006, 2016) = 33%. However, for the purpose of this study, we applied the annual rate of market increase observed from 2015-2016 (2%), considering the inclusion of newer DAA in 2015 and the historical tendency of smaller market increase in years following big changes in treatment guidelines.

**Chart 14 - Estimated public expenditure on hepatitis C medicines in Brazil, 2006 to 2016*.**

| Year | Total expenditures in current values (unadjusted) (BRL) | Total expenditures adjusted to the inflation* (BRL) | Annual variation of public expenditures on hepatitis medicines (%) |
|---|---|---|---|
| 2006 | 33,270,968.71 | 60,759,684.23 | |
| 2007 | 256,493,132.28 | 448,410,508.67 | 638% |
| 2008 | 241,256,933.87 | 398,275,768.88 | -11% |
| 2009 | 226,397,587.44 | 358,302,575.40 | -10% |
| 2010 | 213,405,327.60 | 318,894,056.09 | -11% |
| 2011 | 260,874,119.62 | 366,034,950.74 | 15% |
| 2012 | 239,213,713.38 | 317,123,043.62 | 13% |
| 2013 | 165,318,477.85 | 206,931,286.65 | 35% |
| 2014 | 372,872,988.60 | 438,614,758.43 | 112% |
| 2015 | 945,554,000.84 | 1,005,027,205.75 | 129% |
| 2016 | 1,024,694,075.88 | 1,024,694,075.88 | 2% |

[xxi] 84 tablets per each treatment.

| Year | Total expenditures in current values (unadjusted) (BRL) | Total expenditures adjusted to the inflation* (BRL) | Annual variation of public expenditures on hepatitis medicines (%) |
|---|---|---|---|
| Annual rate of market increase | | | 33% |

* Values adjusted to inflation according to IPCA 2016.
Source: Ministry of Health, Brazil. SIASG for 2006 to 2014, apud Chaves et al. 2017. From 2006 to 2014, the data does not include information about procurement direct from the public manufacturer on ribavirin. For 2015 and 2016, data provided from the Access to Information Law.

The calculation of the average of inclusions and exclusions of medicines for hepatitis C was based on historical data available in the national therapeutic guidelines (Chart 15 and Chart 16). For purpose of the base scenario, we considered those averages for the period of 2017-2051. For 2016, we considered the exclusion of two DAA (boceprevir and telaprevir).

**Chart 15 - Inclusion and exclusion of new medicines for hepatitis C. Brasil, 2000-2016**

| Year | Inclusion | Entry with exclusivity | Exclusion |
|---|---|---|---|
| 2000 | 3 | 0 | - |
| 2001 | - | - | - |
| 2002 | - | - | - |
| 2003 | - | - | - |
| 2004 | - | - | - |
| 2005 | - | - | - |
| 2006 | 2 | 2 | - |
| 2007 | - | - | - |
| 2008 | - | - | - |
| 2009 | - | - | - |
| 2010 | - | - | - |
| 2011 | - | - | - |
| 2012 | 2 | 2 | - |
| 2013 | - | - | - |
| 2014 | - | - | - |
| 2015 | 3 | 3 | - |
| 2016 | - | - | 2 |

**Chart 16 - Average of inclusions and exclusions of Hepatitis C medicines**

| Data | Number | Average of inclusion/exclusion per year |
|---|---|---|
| Number of inclusions 2006 - 2016 | 10 | 0.588235294 |
| Number of exclusions 2006 - 2016 | 2 | 0.117647059 |

From the total of eight medicines available for hepatitis C in 2016, only three were non-exclusive (conventional alfainterferon 2a and 2b and ribavirin) (Chart 17). Ribavirin was the only one identified as locally produced.

**Chart 17 - Assessment of market exclusivity situation for Hepatitis C drugs in 2016 in Brazil**

| Product | Patent status in 2016 | Market situation in 2016 |
|---|---|---|
| Alfainterferon 2a | - | Non-exclusive |
| Alfainterferon 2b | - | Non-exclusive |
| Alfapeginterferon 2a | Granted | Exclusive |
| Alfapeginterferon 2b | Withdrawn | Exclusive (only one producer with market approval and purchases under exclusivity regime) |
| Ribavirin | - | Non-exclusive |
| Boceprevir | Pending patent application | Exclusive |
| Telaprevir | Pending patent application | Exclusive |
| Sofosbuvir | Pending patent application | Exclusive |
| Daclatasvir | Pending patent application | Exclusive |
| Simeprevir | Pending patent application | Exclusive |

In order to estimate the number of API losing patent protection (AOPPi), we considered the oldest granted patent or pending patent application, as shown in Chart 18.

**Chart 18 - Estimate of API losing patent protection**

| Product | Patent number | Estimated expiry (year) |
|---|---|---|
| Alfapeginterferon 2a | PI9703421 | 01/06/2017 |
| Alfapeginterferon 2b | PI9809425 | 27/04/2018 |
| Sofosbuvir | PI0111127-2 | 31/12/2026 |
| Daclatasvir | PI0716483-1 | 08/08/2027 |
| Simeprevir | PI0506945 | 31/12/2026 |

Although in 2016, procurements were only for three exclusive products, there were eight products available for the treatment according to the therapeutic guideline. In the historical data, it can be observed that government purchases medicines in alternate years, considering stocks from previous years. For this reason, we considered the market of 2016 as having eight medicines.

The proportion of sales under exclusivity was based on historical available data (Chart 19). From 2006 to 2016, the exclusive market had been 99-100%, which is a major difference from the ARV market. It is important to highlight that, from the data available, the non-exclusive market-share in terms of sales is nearly residual (Chart 20).

As this data is only used to simulate changes in the domestic industry, which was not applied for the Hepatitis C case, we assumed the share of domestic production as 0%. This does not interfere at all in the simulation of changes in expenditures.

**Chart 19 – Market-share (%) of exclusive and non-exclusive products for Hepatitis C. Brazil, 2006-2016.**

| Product | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Alfainterferona 2a | 1.19 | 0.001 | 0.001 | 0.006 | | | | 0.014 | 0.001 | | |
| Alfainterferona 2b | 1.00 | | | | | | 0.008 | | | | |
| Alfapeginterferona 2a | 97.71 | 39.69 | 51.41 | 49.50 | 99.9987 | 65.18 | 0.014 | 65.92 | 34.71 | | |
| Alfapeginterferona 2b | 1.00 | 60.30 | 48.57 | 50.48 | | 34.81 | | 34.05 | | | |
| Ribavirin | 0.04 | 0.007 | 0.004 | 0.001 | 0.001 | 0.001 | 0.001 | | | | |
| Boceprevir | | | | | | | 21.48 | | | 2.5078 | |
| Telaprevir | | | | | | | 78.48 | | 65.28 | | |
| sofosbuvir | | | | | | | | | | 71.79 | 72.68 |
| daclatasvir | | | | | | | | | | 18.19 | 23.31 |
| simeprevir | | | | | | | | | | 7.49 | 4.00 |
| % non-exclusive | 2.2383 | 0.0087 | 0.0056 | 0.0074 | 0.0013 | 0.0009 | 0.0095 | 0.0143 | 0.0016 | | |
| % exclusive | 98.71 | 99.99 | 99.99 | 99.99 | 99.99 | 99.99 | 99.99 | 99.98 | 99.99 | 100 | 100 |

**Chart 20 – Assumption of market share of hepatitis C according to the market exclusivity situation in 2016**

| | |
|---|---|
| **Market share of API under exclusive market** | 99% |
| **Market share of API on non-exclusive market** | 1% |
| **Market share of domestic industry under exclusive market** | 0% |
| **Market share of domestic industry under non-exclusive market** | 0% |

To estimate the average of price reduction (RPec) after generics enter the market, we considered the prices of generic versions available in the international market, as there were no generics for hepatitis C medicines available in Brazil. If patent barriers were overcome in 2016, the only generic options would have been those from the international market. For this reason, we estimated an average difference (Chart 21) between the price paid by the Brazilian government in 2016 and the price of an Indian generic option (92%; which means brand price if 12.5 times higher than the generic).

**Chart 21 - Estimated price reduction of selected hepatitis C medicines**

| Product | Brazil unit price (2016) BRL | Generic unit price (2016) BRL (1) | Price difference (%) |
|---|---|---|---|
| Sofosbuvir 400mg | 252.92 | 19.19 | 91.88% |
| Daclatasvir 60mg | 93.81 | 7.61 | 92.41% |
| Average reduction | | | 92.14% (rounded to 92%) |

* All prices were adjusted to the inflation according to IPCA 2016
** Exchange rate:US$1= R$3.49
(1) HepCAsia, Generic DAAs pricing, Market price, 2016.

The average time between patent application and regulatory approval (DT) was estimated based on the data of the first market approval in Brazil and the oldest patent application in the country (Chart 22).

**Chart 22 - Time between patent application and market registration (years)**

| Product | Brazilian patent number | Patent application date* | Market registration date | Time lag: patent application / market registration (years) |
|---|---|---|---|---|
| Alfapeginterferona 2a | PI9703421 | 02/06/1997 | 27/12/2001 | 4.57 |
| Alfapeginterferona 2b | PI9809425 | 28/04/1998 | 02/01/2006** | 7.69 |
| Boceprevir | PI0112540 | 19/07/2001 | 25/07/2011 | 10.02 |
| Telaprevir | PI0911673 | 23/04/2009 | 31/10/2011 | 2.52 |
| sofosbuvir | PI0111127 | 23/05/2001 | 27/03/2015 | 10.94 |
| daclatasvir | PI0716483 | 09/08/2007 | 06/01/2015 | 7.42 |
| simeprevir | PI0506945 | 28/01/2005 | 11/03/2015 | 10.12 |
| AVERAGE | | | | 7.61 (rounded to 8) |

*It was considered the oldest patent application in Brazil for each product
**O registro atualmente disponivel na pagina eletronica da Anvisa foi obtido em 03/01/2011. No entanto, o produto foi incorporado no protocolo de tratamento de 2006, o que torna a data de 2011 como incoerente para obtencao do primeiro registro. Portanto, assumimos que o primeiro registro foi obtido em 2006.

All these parameters are summarized in the table below, referring to the various scenarios calculated in the prospective simulation (Chart 23).

**Chart 23 - Prospective simulation, parameters used for Hepatitis C market**

| Fixed param. | Value (base scenario) | (w/o art. 40 ext.) | (data exclus.) | (reg. delay comp.) | (base + data exclusivity + regulatory delay) |
|---|---|---|---|---|---|
| YI | 2016 | 2016 | 2016 | 2016 | 2016 |
| YL | 2051 | 2051 | 2051 | 2051 | 2051 |

| | | | | | |
|---|---|---|---|---|---|
| TAPto | 8 | 8 | 8 | 8 | 8 |
| MVto | BRL 1,024,694,075.88 | BRL 1,024,694,075.88 | BRL 1,024,694,075.88 | BRL 1,024,694,075.88 | BRL 1,024,694,075.88 |
| α | 0.02 | 0.02 | 0.02 | 0.02 | 0.02 |
| d | 0.03 | 0.03 | 0.03 | 0.03 | 0.03 |
| $k_{de}$ | 0 | 0 | 0 | 0 | 0 |
| $k_{dc}$ | 0 | 0 | 0 | 0 | 0 |
| **Scenario-Specific** | **Value (base scenario)** | **(w/o art. 40 ext.)** | **(data exclus.)** | **(reg. delay comp.)** | **(all three cases)** |
| YP | 1997 | 1997 | 1997 | 1997 | 1997 |
| YDP | 2051 | 2051 | 2051 | 2051 | 2051 |
| PD | 20 | 20 | 20 | 20 | 20 |
| DT | 8 | 8 | 8 | 8 | 8 |
| PDE | 4 | 0 | 4 | 9 | 9 |
| pPDE | 0.4 | 0.4 | 0.4 | 0.4 | 0.4 |
| TTC | 0 | 0 | 0 | 0 | 0 |
| DE | 0 | 0 | 5/8 | 0 | 5/8 |
| RPec | 12.5 | 12.5 | 12.5 | 12.5 | 12.5 |
| e | 0 | 0 | 0 | 0 | 0 |
| **Annual Input** | **Value (base scenario)** | **(w/o art. 40 ext.)** | **(data exclus.)** | **(reg. delay comp.)** | **(all three cases)** |
| Ali | 0.58 | 0.58 | 0.58 | 0.58 | 0.58 |
| AOI | 0.11 | 0.11 | 0.11 | 0.11 | 0.11 |
| AIPPi | 0.41 | 0.41 | 0.41 | 0.41 | 0.41 |

**Results: the impact on ARV and Hepatitis C public expenditures and domestic production sales of ARV**

The results were obtained by comparing the base scenario to the alternative scenarios. The base scenario considers the market in 2015 for ARV and in 2016 for Hepatitis C and no change in the IP regulation in Brazil. Therefore, the base scenario includes the patent term extension due to patent examination delay contained in the sole paragraph of article 40 of Brazilian patent law. The period of 35-years was adopted to allow the necessary time for the changes in IPR to take full effect in the pharmaceutical market.

The alternative scenarios in the prospective model were as follows:

a) **Alternative scenario 1** - the absence of the article 40, sole paragraph, related to patent term extension based on patent examination delay;
b) **Alternative scenario 2** – the adoption of patent term extension due to market authorization delay;
c) **Alternative scenario 3** – the adoption of data exclusivity for a period of 5 and 8 years;

d) **Alternative scenario 4** – the adoption of both data exclusivity (5 and 8 years) and patent term extension due to delay in market authorization.

*Base scenario*

**Chart 24 - Base scenario: evolution of ARV expenditures and domestic production market, 2015-2050**

| Year | Proportion of API under exclusivity (pei) | ARV market in expenditures (R$) (MVi) | Domestic production market in sales (R$) (MVDi) |
|---|---|---|---|
| | | Adjusted to inflation | Adjusted to inflation |
| 2015 | 0.36 | 1,119,149,617.60 | 598,236,341.05 |
| 2050 | 0.27 | 2,952,875,834.63 | 1,818,848,610.65 |

The figure of approximately BRL 1.1 billion spent on ARV medicines was obtained from the Brazilian MoH. Considering an average growth of 3% from 2008 to 2015 (adjusted to the inflation), it is estimated that without any change in the current industrial property legislation, the ARV market will nearly triple in 2050 in comparison to 2015. Domestic production sales would have an increase of BRL 1.8 billion in 2050 compared to 2015 (Chart 24).

For Hepatitis C, considering an average growth of 2% in the government expenditures with medicines would go from BRL 1.02 billion in 2016 to BRL 2.49 in 2051 (Chart 25).

**Chart 25 - Base scenario: evolution of hepatitis C expenditures, 2016-2051**

| Year | Proportion of API under exclusivity (pei) | ARV market in expenditures (R$) (MVi) |
|---|---|---|
| 2016 | 0.67 | 1,024,694,075.88 |
| 2051 | 0.25 | 2,049,274,977.03 |

*Alternative scenario 1: Base scenario without the patent term extension due to patent examination delay*

This simulation was conducted in order to estimate the impact on government spending in ARV and hepatitis C and in the participation of domestic production in the ARV market in case of exclusion of the patent term extension due to patent

examination delay provided for under article 40 (sole paragraph) of the Brazilian patent law.

**Chart 26 - Alternative scenario 1: evolution of ARV expenditures and domestic production market, 2015-2050**

| Year | Proportion of API under exclusivity (pei) | ARV market (BRL) | | Domestic production market (BRL) | |
|---|---|---|---|---|---|
| | | Base scenario | Variation in expenditure | Base scenario | Variation in domestic production sales |
| 2015 | 0.36 | 1,119,149,617.60 | | 598,236,341.05 | |
| 2050 | 0.24 | 2,952,875,834.63 | -113,450,287.64 | 1,818,848,610.65 | 609,235.12 |
| Cumulative (2015-2050) | | | -2,054,436,157.85 | | 92,371,220.99 |

If this TRIPS-provision were excluded from Brazilian law, there would be a reduction in total spending with ARV of almost BRL 113 million in 2050 alone. In aggregate, **the reduction between 2015 and 2050 would achieve more than BRL 2.05 billion**. Domestic production would benefit from this change in the patent law, as ARV sales would be BRL 92 millions higher than the base scenario from 2015 to 2050 (Chart 26).

For hepatitis C medicines, savings would be of BRL 747 million in 2051 alone and achieve BRL 16 billion from 2016-2051 (Chart 27).

**Chart 27 - Alternative scenario 1: evolution of expenditures on Hepatitis C medicines, 2016-2051**

| Year | Proportion of API under exclusivity (pei) | Market for Hepatitis C medicines (BRL) | |
|---|---|---|---|
| | | Base scenario | Variation in expenditure |
| 2016 | 0.67 | 1,024,694,075.88 | |
| 2051 | 0.22 | 2,049,274,977.03 | -742,781,710.26 |
| Cumulative (2016-2051) | | | -16,862,109,838.52 |

*Alternative scenario 2: Base scenario with the adoption of patent term extension as consequence of delay in regulatory market authorization*

Alternative scenario 2 assumes the adoption of patent term extension due to delay in obtaining regulatory market approval, as proposed in the EU proposal. In practice, this

is the cumulative effect of the existing patent term extension due to delay in patent examination already contained in the Brazilian law (sole paragraph of article 40) and the extension due to market authorization delay. This scenario assumes there would be patent term extension for market authorization delay beginning in the year 2015 for ARV and in 2016 for Hepatitis C medicines.

As shown in Chart 28, **the cumulative increase in ARV expenditures from 2015 to 2050 would be around BRL 1.25 billion**, while the decrease in the market-share on sales from domestic production would be around BRL 102 million (Chart 28).

For hepatitis C medicines (Chart 29), **the cumulative increase in expenditures from 2016 to 2051 would be around BRL 16 billion**, while the decrease in the market-share on sales from domestic production would be around BRL 102 million.

**Chart 28 - Alternative scenario 2. Evolution of ARV expenditures and domestic production market, 2015-2050**

| Year | Proportion of API under exclusivity (pei) | ARV market (BRL) | | Domestic production market (BRL) | |
|---|---|---|---|---|---|
| | | Base scenario | Variation in expenditure | Base scenario | Variation in domestic production sales |
| 2015 | 0.36 | 1,119,149,617.60 | | 598,236,341.05 | |
| 2050 | 0.29 | 2,952,875,834.63 | 94,541,906.37 | 1,818,848,610.65 | -4,810,604.71 |
| Cumulative (2015-2050) | | | 1,255,011,241.61 | | -102,019,013.39 |

**Chart 29 - Alternative scenario 2. Evolution of expenditures on Hepatitis C medicines, 2016-2051**

| Year | Proportion of API under exclusivity (pei) | Market for Hepatitis C medicines (BRL) | |
|---|---|---|---|
| | | Base scenario | Variation in expenditure |
| 2016 | 0.67 | 1,024,694,075.88 | |
| 2051 | 0.29 | 2,049,274,977.03 | 928,477,137.82 |
| Cumulative (2016-2051) | | | 16,326,989,040.47 |

*Alternative scenario 3: base scenario with the adoption of data exclusivity of 5 or 8 years*

This scenario assumes there would be data exclusivity in Brazil beginning in the year 2015 for ARV market analysis and in 2016 for Hepatitis C medicines. As there is no specific time set in the EU proposal, we considered the minimum time of 5 years established in some FTA and 8 years in others.

From 2015 to 2050, the adoption of 5 years data exclusivity would result in a cumulative **increase in ARV expenditures of BRL 2.4 billion** and a reduction in sales from domestic industry of BRL 237 million. When simulating with the 8 years of data exclusivity, for the same period, the cumulative **increase in ARV expenditures would be of around BRL 3.7 billion** and a reduction in sales of the domestic industry of around BRL 423 million (Chart 30).

From 2016 to 2051, the adoption of 5 years data exclusivity would result in a cumulative **increase in Hepatitis C medicines expenditures of BRL 31 billion**. When simulating with the 8 years of data exclusivity, for the same period, the cumulative **increase in Hepatitis C medicines expenditures would be of around BRL 47 billion** (Chart 31).

**Chart 30 - Alternative scenario 3: Evolution of ARV expenditures and domestic production market, 2015-2050**

| | | ARV market (BRL) | | Domestic production market (BRL) | |
|---|---|---|---|---|---|
| Year | Proportion of API under exclusivity (pei) | Base scenario | Variation in expenditure as consequence of 5 years data exclusivity | Base scenario | Variation in domestic production sales as consequence of 5 years data exclusivity |
| 2015 | 0.36 | 1,119,149,617.60 | | 598,236,341.05 | |
| 2050 | 0.29 | 2,952,875,834.63 | 87,538,802.19 | 1,818,848,610.65 | -4,320,116.33 |
| Cumulative (2015-2050) | | | 2,452,784,149.22 | | -237,064,189.84 |
| Year | Proportion of API under exclusivity (pei) | Base scenario | Variation in expenditure as consequence of 8 years data exclusivity | Base scenario | Variation in domestic production sales as consequence of 8 years data exclusivity |
| 2015 | 0.36 | 1,119,149,617.60 | | 598,236,341.05 | |
| 2050 | 0.30 | 2,952,875,834.63 | 140,062,083.51 | 1,818,848,610.65 | -8,521,953.72 |
| Cumulative (2015-2050) | | | 3,740,179,503.19 | | -423,690,419.73 |

**Chart 31 - Alternative scenario 3: Evolution of expenditures on Hepatitis C medicines, 2016-2051**

| Year | Proportion of API under exclusivity (pei) | Hepatitis medicines market (BRL) | |
|---|---|---|---|
| | | Base scenario | Variation in expenditure as consequence of 5 years data exclusivity |
| 2016 | 0.67 | 1,024,694,075.88 | |
| 2051 | 0.29 | 2,049,274,977.03 | 873,570,516.39 |
| Cumulative (2016-2051) | | | 31,451,189,948.91 |
| **Year** | **Proportion of API under exclusivity (pei)** | **Base scenario** | **Variation in expenditure as consequence of 8 years data exclusivity** |
| 2016 | 0.67 | 1,024,694,075.88 | |
| 2051 | 0.31 | 2,049,274,977.03 | 1,428,806,014.09 |
| Cumulative (2016-2051) | | | 47,861,780,962.03 |

*Alternative scenario 4: Base scenario with the adoption of patent term extension due to market authorization delay and data exclusivity for 5 or 8 years*

This alternative scenario simulates the effect of all previous provisions together. This is what would happen if the EU's proposed text were approved as it is and no other changes are made at the current Brazilian IP law.

Considering 5 years of data exclusivity plus extension of patent term for regulatory delay, **additional spending on ARV would reach BRL 182 million in 2050 alone, and BRL 3.7 billion in aggregate from 2015 to 2050** (Chart 32). Domestic industry sales would reach a decrease of BRL 12 million in 2050 and BRL 393 in aggregate in the same period. If the period of 8 years for data exclusivity were adopted, **there would be BRL 4.99 billion in additional spending from 2015 to 2050 and BRL 612 million in losses for the domestic industry in the same period.**

For hepatitis C market, considering 5 years of data exclusivity plus extension of patent term for regulatory delay, **additional spending would reach BRL 1.7 billion in 2051 alone, and BRL 46 billion in aggregate from 2016 to 2051** (Chart 33). If the period of 8 years for data exclusivity were adopted, **there would be BRL 63 billion in additional spending from 2016 to 2051.**

**Chart 32 - Alternative scenario 4: Evolution of ARV expenditures and domestic production market, 2015-2050**

| Year | Proportion of API under exclusivity (pei) | ARV market (BRL) | | Domestic production market (BRL) | |
|---|---|---|---|---|---|
| | | Base scenario | Variation in expenditure as consequence of patent extension due to market authorization delay + 5 years data exclusivity | Base scenario | Variation in domestic production sales as consequence of patent extension due to regulatory delay + 5 years data exclusivity |
| 2015 | 0.36 | 1,119,149,617.60 | | 598,236,341.05 | |
| 2050 | 0.31 | 2,952,875,834.63 | 182,080,708.56 | 1,818,848,610.65 | -12,752,698.13 |
| Cumulative (2015-2050) | | | 3,707,795,390.84 | | - 393,412,112.51 |
| **Year** | **Proportion of API under exclusivity (pei)** | **Base scenario** | **Variation in expenditure as consequence of patent extension due to market authorization delay + 8 years data exclusivity** | **Base scenario** | **Variation in domestic production sales as consequence of patent extension due to market authorization delay + 8 years data exclusivity** |
| 2015 | 0.36 | 1,119,149,617.60 | | 598,236,341.05 | |
| 2050 | 0.33 | 2,952,875,834.63 | 234,603,989.87 | 1,818,848,610.65 | -19,127,721.77 |
| Cumulative (2015-2050) | | | 4,995,190,744.80 | | - 612,635,671.97 |

**Chart 33 - Alternative scenario 4: Evolution of expenditures on Hepatitis C medicines, 2016-2051**

| Year | Proportion of API under exclusivity (pei) | Base scenario | Variation in expenditure as consequence of patent extension due to market authorization delay + 5 years data exclusivity |
|---|---|---|---|
| 2016 | 0.67 | 1,024,694,075.88 | |
| 2051 | 0.33 | 2,049,274,977.03 | 1,737,270,179.48 |
| Cumulative (2016-2051) | | | 46,639,086,730.75 |
| **Year** | **Proportion of API under exclusivity (pei)** | **Base scenario** | **Variation in expenditure as consequence of patent extension due to market authorization delay + 8 years data exclusivity** |
| 2016 | 0.67 | 1,024,694,075.88 | |
| 2051 | 0.35 | 2,049,274,977.03 | 2,292,505,677.18 |
| Cumulative (2016-2051) | | | 63,049,677,743.86 |

**Discussion of results and Implications for Health Policies**

In 2015, the United Nations Secretary-General established a High Level Panel on Access to Medicines in order to address the policy incoherence between the rights of inventors, international human rights law, trade rules and public health in the context of health technologies. One of the recommendations of the report[11], published in 2016, was as follows:

*"Governments engaged in bilateral and regional trade and investments treaties should ensure that these agreements do not include provisions that interfere with their obligations to fulfil the right to health. As a first step, they must undertake public health impact assessments. These impact assessments should verify that the increased trade and economic benefits are not endangering or impeding the human rights and public health obligations of the nation and its people before entering into commitments. Such assessments should inform negotiations, be conducted transparently and made publicly available" (p.9).*

The HLP also recommends the adoption of measures to avoid undue commercial pressure from the private sector in the negotiation of any change in IPR that can lead to undermining the use of TRIPS flexibilities (p.9), which is the case of some measures proposed by the EU that increases market exclusivity.

The present study aims at providing additional evidence on the effect that adopting the TRIPS-plus provisions proposed by the EU during the negotiations of a free trade agreement with Mercosur could have for guaranteeing universal access to medicines in Brazil.

This study adds to previous ones by allowing a prospective simulation comparing four possible scenarios, including the cumulative effect of TRIPS-plus provisions, with an already TRIPS-plus scenario enforced by the sole paragraph of article 40 in Brazilian industrial property legislation that allows for patent term extension due to delay in patent examination. The present study also provides an estimation of the effect of adopting the data exclusivity provision for a period of 5 and 8 years in ARV expenditures and domestic production sales, as well on hepatitis C medicines expenditures, which has not been done so far by previous studies.

The purpose of analysing two disease groups of medicines is to show the difference between the two markets, from where the simulation starts, and the level of risks that TRIPS-plus provisions might have on each different scenario.

The ARV market and generic competition has been possible thanks to local production, before the adoption of the new patent law, and to the use of public health TRIPS flexibilities – compulsory license and patent oppositions – for some patented medicines. The issue of a compulsory license of efavirenz allowed generic competition 6 years before the patent expiration date. Price reductions of medicines under exclusivity have also been possible thanks to strategies of price negotiations, by using estimates of cost of production by national public laboratories and threats to issue a compulsory license.

The use of patent oppositions for tenofovir patent applications overcame the *de facto* monopoly created by pending applications. It also contributed to the adoption of generic fixed-dose-combinations containing TDF in 2014.

The Hepatitis C market brings a completely different panorama. From 2006 to 2016, its market-share (expenditures) has been almost a 100% with products under exclusivity, with significant increases in expenditures. The most recent one was from 2014 to 2015, from BRL 438.6 million in 2014 to BRL 1 billion in 2015 due to the adoption of the newer DAA sofosbuvir, daclatasvir and simeprevir, with therapeutic regimens costing per treatment USD 8,742 (sofosbuvir+daclatasvir) and USD 8,802 (sofosbuvir+simeprevir).

**The market-share of non-exclusive products has been residual and there have not been generic competition**. In 2016 and 2017, civil society groups and a public manufacturer filed patent oppositions for sofosbuvir patent applications, but so far it has not resulted overcoming patent barriers and promotion of generic competition. **Therefore, the use of public health TRIPS-flexibilities have not resulted in effective generic competition yet.**

Recent estimate assumed that if the 1.4 million people with HCV were eligible for the SOF + DAC treatment (USD 8,732), the resources required to treat everyone in need would be USD 12.2 billion or BRL 40.7 billion. This amount represents 3.3 times the amount the Brazilian Ministry of Health expended on medicines (R$ 12.4 billion) in 2014. Therefore, the prices of the newer DAA are really threatening the commitment of SUS of universal access to treatment [34].

The challenge of ensuring access to hepatitis C medicines are not only for developing countries, but also for developed countries. In France, it was estimated that if all the 127,700 people eligible were treated with sofosbuvir, the cost would be higher than the budget for the Public Hospital System of Paris (Assistance Publique des Hôpitaux de Paris) in 2014 [35]. This is because the cost per treatment when DAA were launched in

France were € 56,000; therefore, the total spending of treatment would reach 7.15 billion Euros.

For the ARV simulation of the impact of Trips-plus provision, the estimates were conservative by adopting an annual growth rate of 3% of the ARV market, which was estimated from ARV expenditures from 2008 to 2015 adjusted to the inflation. This seems coherent, as historical data on ARV expenditures in Brazil has shown that annual spending have been relatively stable against the annual increase of people living with HIV on treatment. However, this is likely to change as of 2013 on, as a new treatment guideline was adopted in the end of 2013 to treat everyone living with HIV regardless of CD4 count. This is already reflected in Chart 4, where the number of people under treatment increasing more in 2014 and 2015 than in previous years.

However, even using a conservative estimation, the results shown in the previous session of the present study are impressive.

Alternative scenario 4 shows the potential impact of the adoption of the EU proposal on the public expenditures only related to ARV in Brazil, which would lead to an increase of BRL 4.9 billion in a 35-years period, or an simple average of BRL 142 million per year (regulatory delay and 8years data-exclusivity). **This is equivalent to the annual public expenditure on health of 100,517 persons in Brazil[xxii].** Considering that the provisions adopted at the FTA would have an impact on all the pharmaceutical market in Brazil, the increase on public expenditures of medicines would be much higher.

When analysing the effects of TRIPS-plus provisions in the **participation of local manufacturers in the ARV market**, relevant information is also obtained with different scenarios simulated by this study. The results show that if both TRIPS-plus provisions were adopted as proposed by the EU, **there would be a decrease in domestic production of BRL 393 million (5 years DE) and BRL 612 million (8 years DE) from 2015 to 2050.**

For hepatitis C market, considering 5 years of data exclusivity plus extension of patent term for regulatory delay, **additional spending would reach BRL 1.7 billion in 2051 alone, and BRL 46 billion in aggregate from 2016 to 2051** (Chart 33). If the period of 8

[xxii] The Brazilian public expenditure on health in the year 2014 was of BRL 1,419.85 (USD 604.20), according to a study publish by the Conselho Federal de Medicina (CFM). Available at: https://portal.cfm.org.br/index.php?option=com_content&view=article&id=25985:2016-02-18-12-31-38&catid=3.

years for data exclusivity were adopted, **there would be BRL 63 billion in additional spending from 2016 to 2051.**

The four alternative scenarios simulated in this study show that all the three TRIPS-plus provisions have negative impact on the sales of domestic produced medicines, besides increasing public expenditures.

The estimative of the effects of TRIPS-plus provisions in the ARV and Hepatitis C markets provides only a snapshot of the implications of those provisions on the market share of domestic production and on the public expenditures of medicines by the public health system, considering that ARV and Hepatitis C medicines are a fraction of the medicines provided by SUS in Brazil.

For example, the Ministry of Health spending with the Specialized Component of Pharmaceutical Services (CEAF), which includes newer and high-price medicines, has increased from BRL 3.5 billion in 2008 to BRL 6 billion in 2015[xxiii]. Spending on immunobiological products has increased from BRL 977 million in 2008 to BRL 2.5 billion in 2015[xxiv]. **If the IPRIA model had been applied to those groups of medicines, the effects of the adoption of TRIPS-plus provisions would be even more impressive**.

In the past years, there has been a significant increase in public spending on medicines, most of which are under exclusivity in Brazil[xxv]. In 2015, the Ministry of Health spending on medicines accounted for 13.7% of its entire budget. While federal spending on medicines increased by 74% from 2008 to 2015 (from BRL 8.5 billion to BRL 14.8 billion[xxvi]), the federal health budget only increased by 36.6% in the same period [23].

While increasing public spending on medicines may reflect an increase in the number of individuals being treated, on the other hand it can also mean an increase in spending on high-price drugs, many of which are under monopolistic situations because they are subject to patent protection (pending patent applications or granted patents).

[xxiii] Values were adjusted to inflation 2016.
[xxiv] Values were adjusted to inflation 2016.
[xxv] Another study under the IBSAccess Project is analysing the exclusivity status of high-cost medicines purchased by the public health system in Brazil. First results are expected to be released by the end of 2017.
[xxvi] Values adjusted to the inflation of 2016 (David et al.2016)

Second, in 2016, a new tax regime was approved (EC 95/2016) and it will freeze for 20 years the primary expenditures from the federal government, directly affecting health financing. The budget will only be adjusted by the inflation and will not follow changes in the Gross Domestic Product (GDP), such as it was in the previous regime. Estimates of losses on federal health financing, considering an increase of 2% of the GDP per year and comparing with the previous tax regime, achieves the total of BRL 415 billion from 2017 to 2036 (an average of BRL 20.7 billion per year)[35]. On the other hand, the present study reveals a scenario of increase in public expenditures due to changes in IPR under negotiation in the FTA with the EU, which has an even more harmful effect in light of cutting in health expenditures.

The effects of TRIPS-plus provisions should not only be measured in terms of changes in medicines expenditures and in domestic production. **The adoption of those provisions will also reduce the policy space for the use of public health TRIPS flexibilities and other complementary initiatives Brazil has relied on to guarantee universal access to ARV treatment since 1990,** including the participation of local production to estimate costs of production and to supply a significant proportion of the ARV.

The reduction on the domestic production as consequence of the adoption of TRIPS-plus provisions can also undermine the efforts in the past years related to the implementation of industrial policies initiatives to stimulate the local production of API and final products.

Admitting the limitations of the present study, the data is still relevant to illustrate the significant impact of TRIPS-plus provisions on access to medicines policies and provides the basis for Brazil to reject all those provisions during negotiations with the EU on the FTA with Mercosur.

The increase in spending, reflecting challenges in the incorporation of high price monopoly medicines, as well as the potential reduction in the federal financing on health bring already a very difficult agenda for achieving sustainability of access to medicines policies. Therefore, any agreement that presents provisions directly affecting those policies must be rejected, considering as a basis the human right to health and the State's assumed obligation to implement progressive policies to fulfil the right to health, and the prohibition of retrocession.

**Recommendations**

The estimated additional expenditure of BRL 4.9 billion in the period of 35 years only for medicines used to treat HIV/Aids and of BRL 63 billion for hepatitis C medicines with the adoption of two of the TRIPS-plus provisions proposed by the EU is clear evidence of the harmful effect of these measures on public policies that aim at fulfilling the right the health in Brazil. The average of BRL 142.7 million of additional expenditures for ARV per year is equivalent to the HIV treatment of 57,975 people per year. Furthermore, the adoption of those measures would also have a negative impact on domestic industry, reducing the sales in the same period and going against national development.

The Brazilian Federal determines the protection of industrial property with the aim of achieving economical and technological development and promoting the social interest (article 5, XXIX). The adoption of the TRIPS-plus measures proposed by the EU are against both of those objectives. Considering the need for coherence between public policies in different areas we recommend the non-adoption of any TRIPS-plus provision that extents market exclusivity by Mercosur in its Free Trade Agreement with the European Union.

We also recommend that the Brazilian government and other countries involved in the negotiation of the FTA conduct an impact study in the field of public health and human rights, as recommended recently by the UN High-Level Panel on Access to Medicines. The impact studies should be conducted transparently and be made publicly available.

The negotiations of the FTA should be transparent and all draft texts and proposals from all parties involved should be publicly disclosed and public consultations should be held to allow the participation of all sectors of society.

Furthermore, we recommend the Brazilian government to make all efforts necessary to exclude TRIPS-plus measures already foreseen in national IP legislation, especially the removal of the provision included in the sole paragraph of article 40 of the patent law that allows for patent term extension due to delay in patent examination due to huge negative impact it has on policies of universal access to health and national development .

**References**

1. Correa CM. Intellectual Property Rights, the WTO and developing countries - The Trips Agreement and Policy Options. London and New York: Zed Books Ltd.; Penang, Malasia: Third World Network; 2000.

2. Sell SK. Private Power, Public Law: The Globalization of Intellectual Property Rights. Cambridge: Cambridge Studies in International Relations; 2003.
3. Sell SK. TRIPS was never enough: Vertical forum shifting, FTAs, ACTA, and TPP. J Intell Prop L. 2010;18:447.
4. Achilladelis B, Antonakis N. The dynamics of technological innovation: the case of the pharmaceutical industry. Res Policy. 2001;30(4):535–88.
5. Bermudez JAZ, Oliveira MA, Chaves GC. New drugs: who can afford them? Cad Saúde Pública [Internet]. 2016 [cited 2017 Mar 13];32. Disponível em:: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0102-311X2016001400301&lng=en&nrm=iso&tlng=en
6. Light DW., Kantarjian H. Market Spiral Pricing of Cancer Drugs. Cancer. 2013 Nov 15;3900–2.
7. Experts in Chronic Myeloid Leukemia. The price of drugs for chronic myeloid leukemia (CML) is a reflection of the unsustainable prices of cancer drugs: from the perspective of a large group of CML experts. Blood. 2013 May 30;121(22):4439–42.
8. The Guardian. Hepatitis C drug delayed by NHS due to high cost. 2015 Jan 20.
9. Correa C. Integrating public health concerns into patent legislation in developing countries [Internet]. South Centre Geneva; 2000 [cited 2015 Feb 25]. Disponível em: http://www.who.int/medicinedocs/pdf/h2963e/h2963e.pdf
10. Chaves GC, Oliveira MA. A proposal for measuring the degree of public health-sensitivity of patent legislation in the context of the WTO TRIPS Agreement. Bull World Health Organ. 2007;85(1):49–56.
11. UN Secretary General (2016). Report of the Secretary-General's High Level Panel on Access to Medicines – promoting innovation and access to health technologies. Available at https://static1.squarespace.com/static/562094dee4b0d00c1a3ef761/t/57d9c6ebf5e231b2f02cd3d4/1473890031320/UNSG+HLP+Report+FINAL+12+Sept+2016.pdf (access on 20/08/2017)
12. Acción Internacional para la Salud; Ifarma. El impacto del TPP en el acceso a los medicamentos en Chile, Peru y Colombia [Internet]. 2013 [cited 2016 Feb 22]. Available from: http://web.ifarma.org/index.php?option=com_content&view=article&id=73:el-impacto-del-tpp-en-el-acceso-a-los-medicamentos-en-chile-peru-y-colombia
13. Cortes G, ME. Intellectual property in the FTA: impacts on pharmaceutical spending and access to medicines in Colombia [Internet]. Misión Salud; IFARMA; 2006 [cited 2016 Feb 22]. Available from: http://web.ifarma.org/images/files/pintelectual/TLC_Colombia_ingles[1].pdf

14. Cortes G, ME, Buenaventura FR, Bernate IR. Impacto de los derechos de propiedad intelectual sobre el precio, gasto y acceso a medicamentos en el Ecuador [Internet]. Fundación Ifarma; OPS; 2010 [cited 2016 Feb 22]. Available from: http://web.ifarma.org/images/files/pintelectual/Impacto_de_los_derechos_de_PI-Ecuador_final_diciembre_2010.pdf
15. Cortes G, ME, Cornejo EM, Bernate IR. Impacto del acuerdo comercial UE-países de la CAN, sobre el acceso a medicamentos en el Perú [Internet]. AIS-LAC, Fundación IFARMA, Fundación Misión Salud, Health Action International; 2009. Available from: http://web.ifarma.org/index.php?option=com_content&view=article&id=56:impacto-del-acuerdo-comercial-ue-paises-de-la-can-sobre-el-acceso-a-medicamentos-en-el-peru&catid=9:propiedad-intelectual&Itemid=29
16. Hernández-González G; Valverde M. Evaluación del impacto de las disposiciones de Adipc plus em el mercado institucional de Costa Rica. 2009. Cinpe, ICTSD, OPS, PNUD. Disponible en http://web.ifarma.org/images/files/pintelectual/final_31_julio_09.PDF (acceso em 22/02/2016)
17. Rathe M, Minaya RP, Guzmán D, Franco L. Estimación del impacto de nuevos estándares de propiedad intelectual em el precio de los medicamentos em la Republica Dominicana. 2009. Fundación Plenitud, ICTSD, OPS. Disponible en http://web.ifarma.org/images/files/pintelectual/informe_final_1.pdf (acceso en 22/02/2016)
18. Rovira, J. (2009). Development of a Model to Assess the Impact of Changes in IPR – available at https://www.ictsd.org/sites/default/files/event/2010/03/guide-to-the-ipria-model.pdf
19. Oliveira MA, Luiza VL, Tavares NUL, Mengue SS, Arrais PSD, Farias MR, et al. Access to medicines for chronic diseases in Brazil: a multidimensional approach. Rev Saúde Pública [Internet]. 2016 [cited 2017 Mar 13];50. Disponível em: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0034-89102016000300303&lng=en&nrm=iso&tlng=en
20. Barros e Castro MT de. Licenciamento Compulsória no Brasil: instituições e políticas [Tese de doutorado]. [Rio de Janeiro]: Universidade Federal do Rio de Janeiro; 2014.
21. Aurea AP, Garcia LP, de Magalhães LC, Filgueiras R, Fernandes C, Santana LR, et al. Programas de Assistência Farmacêutica do Governo Federal: evolução recente das compras diretas de medicamentos e primeiras evidências de sua

eficiência, 2005 a 2008. 2010 [cited 2017 Mar 13]; Disponível em:: http://repositorio.ipea.gov.br/handle/11058/3763

22. Fonseca EM da, Costa N do R. Federalismo, complexo econômico-industrial da saúde e assistência farmacêutica de alto custo no Brasil. Ciência & saúde coletiva. 2015 Apr;20(4):1165–76.
23. David G, Andrelino A, Beghin N. Direito a Medicamentos: avaliação das despesas com medicamentos no âmbito federal do Sistema Único de Saúde entre 2008 e 2015. Brasília: Inesc; 2016.
24. Hasenclever L, Lopes R, Chaves GC, Reis R, Vieira MF. O instituto de patentes Pipeline eo acesso a medicamentos: aspectos econômicos e jurídicos deletérios à economia da saúde. Rev Direito Sanitário. 2010;11(2):164–88.
25. Grupo de Trabalho sobre Propriedade Intelectual (GTPI)/Rebrip. Cálculo estimado do prejuízo monetário causado pela compra de quatro medicamentos selecionados protegidos por patentes pipeline [Internet]. 2011 [cited 2017 Mar 13]. Disponível em:: http://deolhonaspatentes.org/media/file/GTPI%20-%20calculo%20pipeline%20(final).pdf
26. Paranhos J, Hasenclever L, Chaves GC, Cunha G, Mercadante E, Cataldo B, et al. Extensão das patentes e custos para o SUS [Internet]. Rio de Janeiro: IE/UFRJ e ABIA; 2016 [cited 2002 Mar 13]. Disponível em:: http://deolhonaspatentes.org/wp-content/uploads/2016/09/O-custo-da-extens%C3%A3o-das-patentes-para-o-SUS-vf.pdf
27. Chaves GC, Hasenclever L, Osorio-de-Castro CGS, Oliveira MA. Strategies for price reduction of HIV medicines under a monopoly situation in Brazil. Rev. Saúde Pública [Internet]. 2015;49. Disponível em: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0034-89102015000100309&lng=en&nrm=iso&tlng=em (acccess on 16/04/2016)
28. Oliveira, M. A.; Santos, E. M. . Acesso ao tratamento para pessoas vivendo com HIV e Aids no Brasil. In: Nair Teles, Jairo Jacques da Matta, Wanda Espirito Santo. (Org.). Políticas de Controle do HIV/AIDS no Brasil e em Moçambique. 1aed.Rio de Janeiro: Editora Fiocruz, 2016, v. 1, p. 139-168.
29. Fonseca, E.M.; Costa, N. R. Federalism, the Economic-Industrial Health Care Complex and High-Cost Pharmaceutical Assistance in Brazil. Ciência e Saúde Coletiva (Impresso), v. 20, p. 1165-1176, 2015.
30. Ministério da Saúde. Protocolo Clínico e Diretrizes Terapêuticas para Manejo da Infecção pelo HIV em Adultos. 2013
31. Reis, R. Panorama Patentário dos Medicamentos Antirretrovirais no Brasil. Tese de doutorado, Pós-Graduação em Políticas Públicas, Estratégias e Desenvolvimento—Rio de Janeiro: Universidade Federal do Rio de Janeiro, 2012.

32. Villardi, P. Panorama do status patentário e registro sanitário dos medicamentos antiretrovirais no Brasil - implicações para o acesso e a política industrial no BrasilAssociação Brasileira Interdisciplinar de Aids, 2012. Disponível em: http://www.deolhonaspatentes.org.br/media/file/Publica%C3%A7%C3%B5es/Publica%C3%A7%C3%A3o%20Pedro_Final_23OUT.pdf
33. Medicines Patent Pool. Medspal – The medicines patent and licenses database. Available - http://www.medspal.org/ (access on 16/04/2016)
34. Chaves, GC; Osorio-de-Castro, Claudia Garcia Serpa; Oliveira, Maria Auxiliadora . Compras públicas de medicamentos para hepatite C no Brasil no período de 2005 a 2015. Ciencia & Saude Coletiva, v. 22, p. 2527-2538, 2017.
35. Londeix P. New treatments for hepatitis C virus: strategies for achieving universal access. Paris: Médecins Du Monde; 2014.
36. Vieira, FS; Benevides, RPS (2016). O Direito à Saúde no Brasil em Tempos de Crise Econômica, Ajuste Fiscal e Reforma Implícita do Estado. Revista de Estudos e Pesquisas sobre as Américas V.10 N.3 2016. pp. 1-28.

SHUTTLEWORTH FOUNDATION