

Patents, access, and local production of medicines: reflections from experiences in the SUS¹

Patentes, acesso e produção local de medicamentos: reflexões a partir de experiências no SUS

Daniela Rangel Affonso Fernandes^a

 <https://orcid.org/0000-0002-0969-2707>

E-mail: daniela.fernandes@fiocruz.br

Carlos Augusto Grabois Gadelha^a

 <https://orcid.org/0000-0002-9148-8819>

E-mail: carlos.gadelha@fiocruz.br

Jose Manuel Santos de Varge Maldonado^a

 <https://orcid.org/0000-0002-0815-1765>

E-mail: jose.maldonado@fiocruz.br

^aFundação Oswaldo Cruz. Escola Nacional de Saúde Pública Sergio Arouca. Rio de Janeiro, RJ, Brasil.

Abstract

This article aims to contribute to the literature and to the national and global debate on overcoming the polarization related to the legal and administrative aspect of the innovation process, seeking to focus on patents as a conditioning factor of the technological trajectories that enable learning in the productive scope. It was based on a theoretical and political framework related to innovation and access to medicines, especially regarding Intellectual Property rights, and on a critical-reflexive analysis of Intellectual Property instruments used in Productive Development Partnerships (PDP), developed by a public national institute for synthetic drug technology. The results demonstrate the importance of making patent rights compatible with the construction of technological and innovation capacities in the country, which are linked to universal access, especially when they involve products that are intended to treat serious, technologically complex and high-cost diseases. In conclusion, to overcome technological dependence and expand access to medicines in Brazil, the State must seek a balance between public and private interests in the healthcare area, articulate the existing legal instruments and align its health, industry, ST&I and intellectual property policies.

Keywords: National Science, Technology and Innovation Policy; CEIS; Intellectual Property, Public Health Policy, Universal Access.

Correspondence

Daniela Fernandes

Rua Ituverava, 532. Rio de Janeiro, RJ, Brasil. CEP 22775-903.

¹ This article received financial support from the Fiocruz/Fiotec project “Challenges for the Unified Health System (SUS) in the national and global context of social, economic and technological changes - CEIS 4.0” and the CNPq project “Science, Technology and Innovation in Health for the sustainability of the SUS.”

Resumo

Este artigo procurou contribuir para a literatura e para o debate nacional e global sobre a superação de uma polarização relacionada ao aspecto jurídico e administrativo do processo de inovação, procurando se concentrar nas patentes como um fator condicionante das trajetórias tecnológicas que viabilizam o aprendizado em âmbito produtivo. Baseou-se em um arcabouço teórico e político relacionado à inovação e ao acesso a medicamentos, especialmente quanto aos direitos de Propriedade Intelectual, e na análise crítico-reflexiva de instrumentos de Propriedade Intelectual utilizados em Parcerias para o Desenvolvimento Produtivo (PDP), desenvolvidas por um instituto de tecnologia em fármacos sintéticos, público e nacional. Os resultados demonstram a relevância da compatibilização dos direitos de patentes com a construção de uma capacidade tecnológica e de inovação no país, vinculada ao acesso universal, especialmente quando envolverem produtos que se destinam ao tratamento de doenças graves, de alta complexidade tecnológica e de alto custo. Conclui-se que, para superação da dependência tecnológica e ampliação do acesso a medicamentos no Brasil, o Estado deve buscar o equilíbrio entre os interesses públicos e privados na área da saúde, a articulação entre os instrumentos jurídicos legais existentes e o alinhamento entre suas políticas de saúde, industriais, de CT&I e Propriedade intelectual.

Palavras-chave: Política Nacional de Ciência, Tecnologia e Inovação; Ceis; Propriedade Intelectual, Política de saúde pública, Acesso Universal.

Introduction

Although it is not the only condition affecting the production of medicines and health products, patent protection in the pharmaceutical area is the subject of constant debate and study, given the different interests involved (social/economic, collective/individual, for example) and the different perceptions of its impact on innovation and access to health. (Carvalhães, 2022; Chaves; Oliveira; Bermudez, 2021; Oliveira; Santana; Ferreira, 2015; WHO, 2008).

In Brazil, the incorporation of the *Agreement on Trade-Related Aspects of Intellectual Property Rights* (TRIPS Agreement) (WTO, 1994), in 1995, which led to the enactment of the Industrial Property Law (IPL)—Law no. 9.279, of May 14, 1996 (Brazil, 1996)—is indicated by many authors as one of the factors detrimental to the evolution of national pharmanchemicals and pharmaceuticals and, consequently, linked to the increase in dependence on foreign technology (Paranhos; Mercadante; Hasenclever, 2020).

Over the last two decades, one of the Brazilian government's measures to reduce technological vulnerability, balance public and private interests, and increase public access to strategic medicines has been the Productive Development Partnerships (PDP) program, which began in 2009. PDPs are instruments used by the Brazilian Ministry of Health (MoH) to influence private producers, national or foreign, to issue a voluntary license and transfer relevant technologies to a public pharmaceutical institute, also called *Laboratório Farmacêutico Oficial* (LFO - Official Pharmaceutical Laboratory); a process that includes the internalization of the Active Pharmaceutical Ingredient (API) by a national pharmanchemical company (Gadelha; Temporão, 2018). Recently, in order to reinforce this and other essential programs for reducing the vulnerability of the SUS, the State launched the National Strategy for the Development of the Economic-Industrial Health Complex, which has among its objectives the expansion and modernization of the infrastructure of the *Complexo Econômico-Industrial da Saúde* (CEIS - Industrial Health Complex), which is essential for the implementation of PDPs (Brazil, 2023).

Considering the implications of patents for public health, this study sought to understand

their impacts on access to strategic medicines in the Brazilian National Health System (SUS), analyzing the instruments used to enable local production and reduce product costs, using as a field of study the experiences of a relevant federal LFO: Farmanguinhos.

In this scenario, this study aimed to instigate reflections on national initiatives to reduce technological dependence within the scope of CEIS and on the polarization that is concentrated around patents, in view of the tacit nature of knowledge and the dependence on past trajectories (path dependence) established in the national pharmaceutical industry (Dosi, 1982; Vieira; Santos, 2020).

The Farmanguinhos Institute was chosen as a reference because it is the country's largest public producer of synthetic medicines, a pioneer in public-private partnerships to tackle the patent barrier and has the highest number of PDPs approved by the Ministry of Health (Gadelha; Temporão, 2018; Brasil, 2022; Fernandes; Gadelha; Maldonado, 2022), thus being highly representative for the study. Using three of the Institute's partnerships, issues involving patents and other initiatives to make local production viable were identified and critically analyzed, especially in relation to the following legal instruments: compulsory licensing, voluntary licensing, and legal challenges.

Method

This is a qualitative, descriptive study based on a theoretical and political framework related to innovation and Intellectual Property rights. The methodological procedures used were a literature review and analysis of secondary data, using national and international Intellectual Property legislation as a source, especially the TRIPS Agreement and the IPL, publications from the BVS and Scielo scientific databases, focusing on patents and health, and the official Farmanguinhos website. Quantitative data on PDPs were taken from the latest spreadsheets made available by the Secretariat of Science, Technology, Innovation, and Strategic Health Supplies (SCTIE-MS), dated October 2023 (Brasil, 2023).

The research was divided into two stages: first, in order to develop and substantiate the discussions, the flexibilities of TRIPS and other mechanisms

for confronting patent protection were studied. In the second stage, the case studies were presented. The inclusion criteria were: being a Farmanguinhos partnership and containing relevant situations involving patents and the use of a patent protection mechanism. After the selection, three partnerships were analyzed in depth: those referring to Efavirenz, Atazanavir and Sofosbuvir.

Results and discussion

Use of TRIPS Agreement flexibilities and other measures to combat patents in Brazil

With the entry into force of the TRIPS Agreement in 1995, all member countries of the World Trade Organization (WTO) were obliged to amend their national legislation to recognize a minimum standard of protection for intellectual property in all technological fields, including that of pharmaceuticals. However, due to the need to balance the promotion of innovation with the public interest—a hallmark of the world patent system since its creation in the Paris Convention of 1883—and political pressure, especially in developing and less developed countries, TRIPS maintained the permission for signatory states to adopt exceptional measures to limit intellectual property rights in order to meet the public health purposes of each country (WIPO, 1998; Chaves et al., 2007; Paranhos; Mercadante; Hasenclever, 2020).

Among these flexibilities established in the TRIPS Agreement, the following stand out: (1) the use of transition periods; (2) compulsory licenses (article 31); (3) international exhaustion, to facilitate parallel imports (article 6); and (4) experimental use and the Bolar exception (article 30). Table 1 shows their definitions, as well as the indication of the related articles in the TRIPS agreement and in the national legislation. These safeguards allowed for generic versions of medicines to enter the market and stimulated competition, paving the way for price reductions and, consequently, the expansion of access in a context of monopoly (Bermudez, 2021).

Brazil did not take advantage of the time allowed for the implementation of TRIPS—expected to be up

to approximately 10 years—as was seen in the case of India, which resulted in a negative effect on local production, especially that of APIs, which was already in sharp decline as a result of the abrupt commercial opening adopted in the early 1990s (Chaves et al., 2007). In the 1980s, strong threats of retaliation from the United States and other developed countries, together with the neoliberal agenda adopted in the country, led to the implementation of the IPL. Measures even more restrictive than those required of WTO member countries, known as TRIPS-plus measures, were included (Paranhos; Mercadante; Hasenclever, 2020), an example of which is the irresponsible permission to retroactively protect existing patents (a mechanism known as *pipeline*), characterizing Brazil as one of the largest economies that are least active in defending national industry.

Compulsory licensing (CL), unlike voluntary licensing—in which the company that owns the patent can choose to whom the technology will be supplied, define the conditions, and determine the countries that will be able to receive the medicine—does not require the authorization of the owner (Kweitel; Reis, 2007). Some characteristics, however, must be observed for its issuance: before obtaining CL, an attempt must be made to obtain a voluntary license under reasonable conditions; the extent and duration of the license must be limited to the purpose for which they were authorized; and the patent holder must receive adequate remuneration, taking into account the economic value of granting the license in question. These situations vary from country to country and can be established by the internal legislation of WTO member states (Kweitel; Reis, 2007).

Despite the limiting conditions imposed in the TRIPS agreement, CL can be of great value for the industrial and technological development of developing countries and, because of its implications at the heart of patent protection, it is often the most contested instrument. As technological knowledge has a strong tacit dimension, this fact is highlighted in all the literature on innovation, including by

authors who are critical of monopolistic practices in the pharmaceutical market (Cassiolato; Lastres, 2005). The greatest impact of the adoption of this instrument provided for in TRIPS may be the induction of technological collaboration between large companies and local companies, which has proved essential in exemplary cases of success in PDPs, as in that of enabling the local production of COVID-19 vaccines (Gadelha; Temporão, 2018; Lima; Gadelha, 2021, Fernandes; Gadelha; Maldonado, 2023).

However, one cannot fall for the myth that the legal dimension alone has the capacity to change reality and global technological asymmetries, which structurally depend on the unequal distribution of global technological and productive capacity (Gadelha; Vargas; Alves, 2019). There are, therefore, limits to how CL alone can enable structural situations of dependency to be overcome in CEIS, given that Brazil, just like the vast majority of countries and regions, lacks technological capacity in a number of fields that are critical to innovation in health (Nonaka; Von Krogh, 2019). However, the use of this instrument should never be ruled out as a possibility when the interests of public health are threatened.

Alternatives to CL, with the possibility of complementary adoption in contexts of proven public interest, are parallel imports (article 6) and the Bolar exception (article 30). These measures are very useful for tackling the vulnerability of public health systems, as described in Table 1. Parallel importation favors access to medicines, as it allows them to be imported at a lower price, regardless of where they are being sold; and the Bolar exception represents one of the ways to seek a balance between the social and commercial function of a patent, since it allows the country to take advantage of the information revealed by the patent holder for the exclusive purpose of producing data and information necessary to obtain a sanitary registration, providing the possibility of making the generic version available to society shortly after the patent for the product expires (Riess, 2020).

Table 1 - Flexibilities of the TRIPS agreement/Legislation

Flexibility	Article TRIPS	Related article in the IPL	Description
Transition periods	nº 65 and 66	nº 243	one year (until 1996) for developed countries, five years (until 2000) for developing countries, 11 years (until 2006) for less developed countries. Developing countries were also granted an additional five years to protect intellectual property in technological fields not previously protected.
Compulsory Licensing	nº 31	nº 68	Government authorization, which allows third parties to exploit a patented product or process without the consent of the patent holder. TRIPS foresees the following hypotheses for the concession: (1) public interest; (2) abuse of the right to exploit the patent; and (3) abuse of economic power.
Exhaustion of rights / parallel imports	nº 6	nº 43 inc. IV and nº 68 paragraph 4	Countries can implement national or international exhaustion of rights. In the national case, the exclusive right is exhausted only in the country where the product was placed on the domestic market by the owner or with their consent. In the international case, a country can import a patented product once it has already been placed on the market by the patent holder or by a third party with their consent.
Exceptions to the Rights Conferred (Experimental Use and Bolar Exception)	nº 30	nº 43, inc. VII	Experimental use refers to the possibility of exploiting a patented object for scientific research purposes. The Bolar exception allows tests to be carried out in order to obtain marketing registration with regulatory agencies before the patent expires, with the aim of obtaining approval to market the generic.

Source: Prepared by the authors based on Chaves et al. (2007); Oliveira, Sant'anna and Ferreira (2015)

In addition to the safeguards described above, the patent examination subsidy, also known as opposition, can be used as long as there is still no final decision on the patent. This mechanism used in Brazil to deal with the patent barrier is described in article 31 of the IPL (Brasil, 1996), allowing third parties interested in the technology to present technical arguments to the National Institute of Industrial Property (INPI), which will serve as input for the final opinion of the patent examiner. This measure aims to prevent the granting of a monopoly when the patentability requirements (novelty, inventive step, and industrial application) are not met and also to prevent evergreening, which is the overlapping of patent applications for medicines, intensifying the situation of indefinite exclusivity (Villardí, 2018).

Still within this general complex context, which involves everything from the legal and political dimension to industrial and innovation policy efforts aimed at structurally altering global asymmetries in health, the PDP program stands out, considered by health experts to be an alternative mechanism to compulsory licenses. The model makes patent rights compatible with the construction of a technological and innovation capacity linked to universal access in the country. Because the patent is not challenged, but voluntary licensing of strategic technologies for the country is encouraged, the PDP is a win for all the players involved and has been the main instrument for tackling the patent barrier and reducing vulnerability in the SUS.

Farmanguinhos cases involving patents and countermeasures

Over the last two decades, Farmanguinhos has been making agreements with private companies and other public laboratories, using PDPs, which have proved to be strategic for transferring technology and know-how, as an instrument. As of November 2021, the Institute had 24 partnerships approved by the MoH. Some of them were terminated for reasons such as partners giving up due to the lack of prospects for centralizing the purchase of a drug or the drug not being incorporated as a therapeutic option in the Clinical Protocol and Therapeutic Guidelines (PCDT), while 13 are still in force. Of these, six were underway (phases II and III) and seven were at the stage of verifying the internalization of technology (phase IV)² in October 2023 (Brazil, 2023).

PDPs follow the theoretical framework of CEIS, guided by a systemic vision focused on social needs, technological vulnerability in health and the use of the state's purchasing power as factors that strongly induce patent holders to voluntarily sign agreements to transfer drug technologies and strategic health products to the country (Gadelha, 2003). As they induce technological development by stimulating the transfer of technology via public-private partnerships, they allow the regular exercise of the right to exploit the patent, standing out as instruments for mitigating the harmful effects of the incidence of patent protection in the healthcare area, particularly in terms of access to medicines (Oliveira; Sant`anna; Ferreira, 2015).

In this model, technical information must necessarily be transferred to an LFO and cover all the information, whether or not it is patented or confidential, relating to the production process of

the drug held by the company (Fernandes; Gadelha; Maldonado, 2023). The agreements generally cover medicines with patents in force and technology transfers negotiated via voluntary licensing.

Given the systemic nature of the model and the lack of innovation in the national pharmaceutical industry, political and management challenges are faced by partners when implementing PDPs, affecting the expected results. In this context, greater investment in infrastructure and training for national technology recipients, especially LFOs, and the role of the MoH in monitoring technology absorption, are seen as necessary for partnerships to generate more effective results and consolidate themselves as instruments for articulating the social and economic dimensions of development (Chaves; Oliveira, 2018; Gadelha; Temporão, 2018; Fernandes; Gadelha; Maldonado, 2023).

For this study, three of the Institute's partnerships were chosen because they have relevant issues in understanding the challenges of using measures to make local production viable for the SUS, in view of existing patent protection. Table 2 shows the different cases and legal instruments analyzed. In the first case, the Efavirenz partnership, which took place even before the PDP legal framework, and which, along with the vaccine strategy, was a precursor to the current PDP model (Gadelha; Temporão, 2018), a successful scenario involving a compulsory license is presented. In the second and third cases, related to the Atazanavir and Sofosbuvir PDPs, respectively in phase IV and II of evolution, some of the challenges and benefits of using a voluntary license and an opposition to the examination of a patent application are presented. In this way, it was intended to provide examples of different instruments for tackling patent barriers and overcoming technological dependence (Oliveira; Sant`anna; Ferreira, 2015), highlighting the importance of using alternatives to reduce vulnerability in public health and strengthen national capacity.

² The process of establishing and executing PDPs is divided into four phases: Phase I - analysis and decision on the PDP project proposal by the MoH, signing of the term of commitment; Phase II - start of implementation of the approved proposal, signing of the agreement between the public institution (PI) and the private company, start of industrial and technological development and training, publication of the sanitary registration of the drug for the private and/or public partner; Phase III - effective transfer and absorption of technology, signing of the contract for the acquisition of the strategic product between the MoH and the PI; and Phase IV - completion of the process, verification of the internalization of the technology (Fernandes, 2019; Brasil, 2023).

Table 2 - PDP/Partner and instrument for dealing with patent barriers

Medication	Partner(s)	Legal instrument
Efavirenz	Globequímica (SP), Cristália (SP), and Nortec (RJ)	Compulsory Licensing
Atazanavir	Bristol-Myers Squibb (BMS)	Voluntary Licensing
Sofosbuvir	Blanver Farmoquímica e Farmacêutica S.A. and Microbiológica Química e Farmacêutica LTDA	Patent opposition

The Case of the Efavirenz CL

One of the most relevant cases involving intellectual property in the laboratory took place in 2007, before the approval of the first public-private partnerships for the transfer of drug technology in Brazil (Chaves; Oliveira, 2018).

In a groundbreaking way, a PDP model was created and associated with the compulsory licensing of the Efavirenz patent, which belonged to the Merck Sharp & Dohme laboratory. The fact that Farmanguinhos already had experience in the production of antiretrovirals, being the largest public producer for the National STD/AIDS Program, enabled it to carry out P&D activities aimed at development, in partnership with national and Indian generic pharmaceutical companies, allowing for the compulsory license of the Efavirenz patent to have effective consequences for access to AIDS treatment. Some factors influenced the Brazilian government to issue the CL: the difficulty of negotiating with the MSD laboratory, which held the patent, to revise its prices for the Brazilian market; international experiences of using CL as an instrument of induction and pressure from civil society, especially from groups linked to health and human rights (Kweitel; Reis, 2007; Póvoa, 2021).

In view of the facts and the importance of Efavirenz for HIV treatment, it was considered a case of public interest, and compulsory licensing was allowed (Póvoa, 2021), as established in article 71 of the Industrial Property Code (Brasil, 1996).

The accumulated knowledge of Farmanguinhos allowed the drug to be developed by reverse engineering, and about a year and nine months after the CL of the patent, its production was completely verticalized. The formulation of the generic version was possible thanks to a public-private partnership in which Farmanguinhos developed the technology

and final production of the drug, and the consortium signed by the private companies Globequímica (SP), Cristália (SP), and Nortec (RJ) was responsible for manufacturing the active ingredient (Póvoa, 2021).

This led to the creation of what became a pilot PDP experience, involving the establishment of a link between Fiocruz and national pharmaceutical laboratories capable of reproducing and transferring the technology of the product (Gadelha; Temporão, 2018; Póvoa, 2021).

Compulsory licensing allows the country to import generic versions from laboratories pre-qualified by the WHO. Therefore, in order to avoid the risk of a shortage of medication for patients during this period, the Ministry of Health signed a contract with Indian suppliers to purchase the generic drug (Rodrigues; Soler, 2009). Despite being a legal measure and having already been implemented in countries such as Canada, Thailand, and Italy, the compulsory licensing of a patented drug was an unprecedented measure in Latin America, and it was taken by the Brazilian government after long and difficult negotiations with the laboratory holding the patent (Chaves; Vieira; Reis, 2008; Rodrigues; Soler, 2009).

This case highlights the importance of state intervention in satisfying the collective social interest in guaranteeing access to health innovation and demonstrates the efficient use of a legal Intellectual Property (IP) resource by an LFO. Although the drug has no longer been part of the protocol for the disease since 2016 and its acquisition has been reduced, the production of Efavirenz is considered a milestone for national public health and for the technological strengthening of Farmanguinhos. The application of this flexibility in the TRIPS agreement also allowed the country to achieve international visibility and gain bargaining

power to negotiate prices for other medicines considered strategic (Oliveira, 2020).

The case of the Voluntary Licensing of Atazanavir

This case began, in 2011, when Farmanguinhos signed a voluntary licensing agreement with Bristol-Myers Squibb (BMS) for the technology transfer of the antiretroviral drug Reyataz, of which an active ingredient is Atazanavir Sulfate, widely used in the treatment of patients with AIDS/HIV. The PDP agreement referred to the pharmaceutical forms of 200 and 300 mg (Chaves; Oliveira, 2018) and encompassed the transfer of technology, manufacture, and distribution of the drug during the period of the agreement, also including, as a requirement, the transfer of API technology to a national private pharminochemical industry, Nortec Química, in order to guarantee the entire production chain of the drug in Brazilian territory (HIV/AIDS..., 2014).

The agreement was signed in 2011, but the sanitary registration was only granted to Farmanguinhos/Fiocruz in January 2014, which delayed the start of the transfer phase and the distribution of the finished drug to SUS (Phase III). Thus, the technological absorption, which had a deadline of five years to be completed, was concluded in June 2020, three years after the patent expired in Brazil, which occurred in 2017 (Silveira; Corrêa; Barroso, 2016; Oliveira, 2020). It should be clarified that obtaining registration is a fundamental stage of PDPs, since it is from there that commercialization is authorized, which enables the acquisition of the finished product from the private partner and distributing it to the SUS, initiating the technology transfer process.

The partnership involved a monopoly drug license. In addition, it faced the challenge of negotiating clauses with the patent holder in order to enable the strategy of internalizing the technology in the country and obtaining the drug at a more affordable price for the SUS; which was made possible by establishing the PDP, despite the existence of limitations for reducing the price after the patent expires and for producing other presentations or combinations in fixed doses (Chaves et al., 2015).

Despite some limitations and the long time taken to incorporate the technology in Brazil, which is

common to many PDP projects, considering the high and risky transaction costs (Williamson, 1985) of these contracts, the partnership enabled Farmanguinhos to enter a new technological activity that is essential for preserving its presence in the production of antiretrovirals and the manufacturing of the API in Brazil, favoring the entire production chain of the drug.

Voluntary licensing, via technology transfer agreements, even in the face of the complexity and difficulties involved, is an instrument to be used as an alternative to CL, to strengthen local production and guarantee access to healthcare. However, there is a need for greater qualification in Science, Technology, and Innovation (ST&I) of the use in conjunction with other strategies to address patent barriers, as the situation requires (Chaves et al., 2015), aiming, among other factors, to overcome technological dependence and the development of CEIS.

The Sofosbuvir patent opposition case: a legal deadlock for local production

The last case to be analyzed, which is of great notoriety and reveals a legal deadlock for local production, is that of the PDP for the Hepatitis C treatment drug Sofosbuvir. Brazil, just like other countries that have included this drug in their lists of medicines for treating the disease, has adopted strategies against the patent barrier to ensure that the population has access to the drug. The cost of this treatment, which in 2015 was USD 84,000 per patient, led the Brazilian government to begin negotiations to reduce the price with Gilead Sciences Ind, a US pharmaceutical company that had filed a patent application for Sofosbuvir in Brazil (PI0410846-9). However, the cost of the negotiation, USD 7,500, is still too high for the SUS budget (Petrov, 2020).

Thus, Farmanguinhos, together with the national laboratories Blanver Farmoquímica e Farmacêutica S.A. and Microbiológica Química e Farmacêutica LTDA, formed a PDP Agreement for the development of the product, which was approved by the Ministry of Health in December 2017. In July 2018, the laboratory obtained the registration of the drug and was now ready to distribute the generic to

the SUS. At the end of the five-year agreement, which would take the form of a reverse transfer (starting with the final stage—quality control analysis and packaging), the laboratory would be able to produce the drug in its industrial complex. With national production, it is estimated that there could be huge savings for the public purse (the cost would be just over R\$5,000 per patient), which would enable more people to have access to treatment (Matos, 2018).

The high cost of the drug, in addition to the strategy of forming the agreement, the lack of patentability requirements, and the absence of descriptive sufficiency, led Farmanguinhos and other institutions to challenge the granting of the patent for the antiviral, presenting subsidies for the examination of the application. However, in September 2018, Gilead obtained a favorable decision from the INPI on the patent application for the drug Sofosbuvir, gaining exclusive production and marketing rights in Brazil. Of the 126 claims filed by Gilead, only two met the legal requirements for concession, according to the authority. However, even for a small number of claims, the effects of the monopoly granted were felt. One of the patents granted referred to an intermediate molecule for the synthesis of the drug, and even though Fiocruz and the BMK Consortium informed that this molecule would not be used for the production of the API under the cooperation agreement, the PDP was suspended by court order, due to a lawsuit filed by Gilead (Matos, 2018; Petrow, 2020).

Despite what happened, it is understood that the presentation of subsidies for the examination of the patent application to the INPI was of crucial importance in ensuring that Gilead did not obtain more protection than it should have (Petrow, 2020). Currently, according to the latest PDP status update spreadsheet made available by SCTIE/MS (Brazil, 2022), the PDP is no longer suspended; however, the issue is still under discussion and the patent is still valid, impacting on local production and the marketing of the drug at an affordable price.

Final considerations

This work shows the tension between intellectual property and the public interest and, at the same time, the possibilities for progress from

a perspective in which the capacity for learning and local production are essential factors for the particular legal forms of the global and national patent protection framework, including the existing flexibilities, to be compatible with overcoming dependence and with the sustainability of strategic SUS programs in the pharmaceutical area.

Furthermore, the recent national and global context of intellectual property in health; the historical framework of PDPs, as the most innovative recent policies for local production in CEIS, despite the learning process and the need for conceptual and public policy advances; and the exemplary cases from Farmanguinhos clearly demonstrate the relevance of the issue and the alternatives involved in making intellectual property rights compatible with the construction of technological and innovation capacities in the country, which are linked to universal access, especially since they involve products intended to treat serious, technologically complex, and expensive diseases, such as AIDS and Hepatitis C.

This research has therefore sought to advance the literature by showing that in order for an intellectual property system to be favorable to the local pharmaceutical industry, in addition to an adequate political and legal framework with regard to patents and other regulatory dimensions, it is necessary to invest heavily in local production and ST&I, in the qualification of professionals, in permanent learning infrastructure in technological and productive platforms and in innovation management procedures, including technology transfers, the result of PDPs, technological orders and other mechanisms involving the purchasing power of the state, associated with local production.

In conclusion, in order to overcome technological dependence and increase access to medicines in Brazil, faced with the enormous challenge of maintaining the sustainability of the SUS, the state must seek a balance between public and private interests in the healthcare area and the articulation between existing legal instruments, under the direction of a national strategy that prioritizes comprehensive and equitable access and alignment between its health, industrial, ST&I and Intellectual Property policies.

References

- BERMUDEZ, J. *Licença compulsória para medicamentos e vacinas em debate*. Entrevistador: Felipe Leonel. Rio de Janeiro: Fiocruz, 12 jul 2021. Entrevista concedida ao Centro de Estudos Estratégicos- CEE-Fiocruz. Disponível em: <<https://cee.fiocruz.br/?q=Licenca-compulsoria-para-medicamentos-e-vacinas-em-debate>>. Accessed on: 5 mar 2022.
- BRASIL, Ministério da Saúde. *Parcerias para o Desenvolvimento Produtivo - PDP*. Brasília, DF, 2022. Disponível em: <<https://www.gov.br/saude/pt-br/composicao/sectics/deciis/pdp>>. Accessed on: 2 out 2023.
- BRASIL. Ministério da Saúde. *Estratégia nacional para o desenvolvimento do complexo econômico-industrial da saúde*. Brasília, DF: 2023. Disponível em <<https://www.gov.br/saude/pt-br/assuntos/noticias/2023/setembro/arquivos/26-09-2023-apresentacao-complexo-economico-industrial-da-saude-versao-final.pdf>>. Accessed on: 25 nov. 2023.
- BRASIL. Lei n. 9.279, de 14 de maio de 1996. Regula direitos e obrigações relativos à propriedade industrial. Brasília, DF: Presidência da República, 1996. Disponível em: <https://www.planalto.gov.br/ccivil_03/leis/l9279.htm>. Accessed on: 2 out 2023.
- CARVALHÃES, E. Quebra de patentes: O que está em jogo? *Interfarma*, São Paulo, 2022. Disponível em: <<https://www.interfarma.org.br/space/artigo-quebra-de-patentes-o-que-esta-em-jogo/>>. Accessed on: 27 nov 2023.
- CASSIOLATO, J. E.; LASTRES, H. M. M. Sistemas de inovação e desenvolvimento: as implicações de política. *São Paulo em Perspectiva*, São Paulo, v. 19, n. 1, p. 34-45, 2005. DOI: 10.1590/S0102-88392005000100003
- CHAVES, G. C.; OLIVEIRA, M. A. Estratégias governamentais para redução de preços de medicamentos em situação de monopólio: produção local e enfrentamento da barreira patentária. In: HASENCLEVER, L. et al. *Vulnerabilidades do complexo industrial da saúde: reflexos das políticas industrial e tecnológica na produção local e assistência farmacêutica*. Rio de Janeiro: E-papers, 2018. p. 181-211.
- CHAVES G.V.; OLIVEIRA M.A.; BERMUDEZ, J. Brazil - Patent Barriers and Access to Medicines Through the Public Health System. In: SRIVIDHYA, R; VANNI, A. (Ed.). *Intellectual Property Law and Access to Medicines - Trips Agreement, Health and Pharmaceuticals*. London: Routledge, 2021. p. 147-171
- CHAVES, G. C. et al. A evolução do sistema internacional de propriedade intelectual: proteção patentária para o setor farmacêutico e acesso a medicamentos. *Cadernos de Saúde Pública*, Rio de Janeiro, v. 23, n. 2, p. 257-267, 2007. DOI: 10.1590/S0102-311X2007000200002
- CHAVES, G. C. et al. Strategies for price reduction of HIV medicines under a monopoly situation in Brazil. *Revista de Saúde Pública*, São Paulo, v. 49, 2015. DOI: 10.1590/S0034-8910.2015049005459
- CHAVES, G. C.; VIEIRA, M. F.; REIS, R. Acesso a medicamentos e propriedade intelectual no Brasil: reflexões e estratégias da sociedade civil. *Sur. Revista Internacional de Direitos Humanos*, São Paulo, v. 5, n. 8, p. 170-198, 2008. DOI: 10.1590/S1806-64452008000100009
- DOSI, G. Technological paradigms and technological trajectories. *Research Policy*, Amsterdam, v. 11, n. 3, p. 147-162, 1982. DOI: 10.1016/0048-7333(82)90016-6
- MATOS, A. Farmanguinhos obtém registro do antiviral sofosbuvir, usado contra hepatite C. *Farmanguinhos*, Rio de Janeiro, 5 jul. 2018. Disponível em: <<https://www.far.fiocruz.br/2018/07/farmanguinhos-obtem-registro-do-antiviral-sofosbuvir/?print=print>>. Accessed on: 1 nov. 2023.
- OLIVEIRA, V. Farmanguinhos conclui absorção tecnológica do Atazanavir. *Farmanguinhos*, Rio de Janeiro, 15 jun. 2020. Disponível em: <<https://www.far.fiocruz.br/2020/06/farmanguinhos-conclui-absorcao-tecnologica-do-atazanavir/>>. Accessed on: 14 nov. 2023.
- HIV/AIDS: Fiocruz dá novo passo para a produção do antirretroviral Atazanavir. *Farmanguinhos*,

- Rio de Janeiro, 14 jan. 2014. Disponível em: <<https://portal.fiocruz.br/noticia/hivaids-fiocruz-da-novo-passo-para-producao-do-antirretroviral-atazanavir>>. Accessed on: 24 jan 2023.
- FERNANDES, D. R. A.; GADELHA, C. A. G.; MALDONADO, J. M. S. V. Estratégias de inovação em medicamentos e vacinas no âmbito do Ceis - modelos, mecanismos e expectativas. *Saúde em Debate*, Rio de Janeiro, v. 47, n. 138, p. 377-392, 2023. DOI: 10.1590/0103-1104202313801
- FERNANDES, D. R. A.; GADELHA, C. A. G.; MALDONADO, J. M. S. V. O papel dos produtores públicos de medicamentos e ações estratégicas na pandemia da Covid-19. *Saúde em Debate*, Rio de Janeiro, v. 46, n. 132, p. 13-29, 2022. DOI: 10.1590/0103-1104202313801
- FERNANDES, D. R. A. *Fatores críticos de sucesso em Parceria para o Desenvolvimento Produtivo PDP Estudo de caso em um laboratório farmacêutico público* (Farmanguinhos). Dissertação (mestrado) - Fundação Oswaldo Cruz, Escola Nacional de Saúde Pública Sergio Arouca, Rio de Janeiro. 2019.
- GADELHA, C. A. G. O complexo industrial da saúde e a necessidade de um enfoque dinâmico na economia da saúde. *Ciência & Saúde Coletiva*, Rio de Janeiro, v. 8, n. 2, p. 521-535, 2003. DOI: 10.1590/S1413-81232003000200015
- GADELHA, C. A. G.; VARGAS, M. A.; ALVES, N. G. Pesquisa translacional e sistemas de inovação na saúde: implicações para o segmento biofarmacêutico. *Saúde em Debate*, Rio de Janeiro, v. 43, n. spe2, p. 133-146, 2019. DOI: 10.1590/0103-11042019S210
- GADELHA, C. A. G.; TEMPORÃO, J. G. Desenvolvimento, Inovação e Saúde: a perspectiva teórica e política do Complexo Econômico-Industrial da Saúde. *Ciência & Saúde Coletiva*, v. 23, n. 6, p. 1891-1902, 2018. DOI: 10.1590/1413-81232018236.06482018
- KWEITEL, J.; REIS, R. A primeira licença compulsória de medicamento na América Latina. *Pontes*, Rio de Janeiro, v. 3, n. 3, p. 26-28, 2007.
- LIMA, N. T.; GADELHA, C. G. The COVID-19 Pandemic: Global Asymmetries and Challenges for the Future of Health. *China CDC Weekly*, Beijing, v. 3, n. 7, p. 140-141, 2021. DOI: 10.46234/ccdcw2021.039
- NONAKA, I.; VON KROGH, G. Tacit knowledge and knowledge conversion: controversy and advancement in organizational knowledge Creation Theory. *Organization Science*, [s.l.], v. 20, n. 3, p. 635-652, 2009.
- OLIVEIRA, C. S.; SANT'ANNA, L. S.; FERREIRA, A. P. Licença compulsória e a parceria de desenvolvimento produtivo: assegurando o direito à saúde no Brasil. *Revista Jurídica da Presidência*, Brasília, DF, v. 17, n. 112, 2015.
- PARANHOS, J.; MERCADANTE, E.; HASENCLEVER, L. O custo da extensão da vigência de patentes de medicamentos para o Sistema Único de Saúde. *Cadernos de Saúde Pública*, Rio de Janeiro, v. 36, n. 11, e00169719, 2020. DOI: 10.1590/0102-311X00169719
- PETROW, A. G. Estratégia de depósito de patentes no setor farmacêutico e o enfrentamento por subsídios ao exame de pedidos de patente no Brasil: o caso Sofosbuvir. 2020. 102 f. Dissertação (Mestrado Profissional em Gestão, Pesquisa e Desenvolvimento na Indústria Farmacêutica) - Instituto de Tecnologia em Fármacos, Fundação Oswaldo Cruz, Rio de Janeiro, 2020.
- PÓVOA, L. *Licença compulsória de patentes para o combate à covid-19: limitações, cenários e janela de oportunidade*. Brasília, DF: Núcleo de estudos e pesquisas: CONLEG: Senado, 2021. Disponível em: <<https://www12.senado.leg.br/publicacoes/estudos-legislativos/tipos-de-estudos/textos-para-discussao/td297>>. Accessed on: 18 jan 2023.
- RIESS, E. Exceção Bolar (art. 43, inciso VII da LPI): limite finalístico e temporal. *Revista da ABPI*, Rio de Janeiro, n. 165, 2020.
- RODRIGUES, W. C. V.; SOLER, O. Licença compulsória do efavirenz no Brasil em 2007: contextualização. *Revista Panamericana de Salud Publica*, Washington, v. 26, n. 6, p. 553-559, 2009.

SILVEIRA, C. C. F.; CORRÊA, M. C. D. V.; BARROSO, W. B. G. Estratégia de proteção de patentes farmacêuticas: o caso do atazanavir. *Revista Eletrônica de Comunicação, Informação & Inovação em Saúde*, Rio de Janeiro, v. 10, n. 1, 2016. DOI: 10.29397/reciis.v10i1.1047. DOI: 10.29397/reciis.v10i1.1047

VIEIRA, F. S; SANTOS, M. A. B. *Texto para discussão 2615: o setor farmacêutico no Brasil sob as lentes da conta-satélite de saúde*. Brasília, DF Ipea; 2020.

VILLARDI, P. Ativismo, políticas públicas e acesso a medicamentos: o uso de oposições a pedidos de patentes por organizações da sociedade civil. *Physis: Revista de Saúde Coletiva*, Rio de Janeiro, v. 28, n. 1, e280107, 2018.

WHO - WORLD HEALTH ORGANIZATION. *Resolution WHA61.21: global strategy and plan of action on public health, innovation and intellectual property*. Genebra, 2008.

WILLIAMSON, O. *The economic institutions of capitalism*. New York: Free Press, 1985.

WILLIAMSON, O. Economics and organization: a primer. *Califórnia Management Review, Berkeley*, v. 38, n. 2, p. 131-146, 1996. DOI:10.2307/41165836

OMPI - ORGANIZAÇÃO MUNDIAL DE PROPRIEDADE INTELECTUAL. *Convenção de Paris para a Proteção da Propriedade Industrial*. Genebra, 1998. Disponível em: https://www.wipo.int/edocs/pubdocs/pt/wipo_pub_201.pdf. Accessed on: 26 nov 2023.

WTO - WORLD TRADE ORGANIZATION. *Agreement on Trade-Related Aspects of Intellectual Property Rights* (unamended). Marrakesh, 1994. Disponível em: https://www.wto.org/english/docs_e/legal_e/27-trips_01_e.htm. Accessed on: 20 nov 2023.

Authors' contributions

Daniela Fernandes contributed to the conception, planning, data collection and writing of the paper. Carlos Gadelha contributed to the supervision of the study, writing, analysis, and critical review of the manuscript. Jose Maldonado contributed to the analysis and critical review of the manuscript.

Received: 19/10/2022

Resubmitted: 8/29/2023; 12/11/2023

Approved: 12/27/2023