Innovation strategies in medicines and vaccines within the scope of CEIS – models, mechanisms, and expectations

Estratégias de inovação em medicamentos e vacinas no âmbito do Ceis – modelos, mecanismos e expectativas

Daniela Rangel Affonso Fernandes[1], Carlos Augusto Grabois Gadelha[2], Jose Manuel Santos de Varge Maldonado[2]

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ABSTRACT The article aimed to present relevant and original information about the innovation strategies used by Official Pharmaceutical Laboratories (LFO) to reduce the vulnerabilities of the Brazilian Unified Health System (SUS) and the productive and technological capacity of the Health Economic-Industrial Complex. The methods used included a literature review and the analysis of primary data from interviews conducted in two of the largest LFOs in the country. Their efforts and results in Research and Development (R&D) and incorporation of medicines and vaccine technologies were identified and analyzed, with emphasis on Productive Development Partnerships (PDP). Although R&D activities still need to advance, benefits were brought about by technology transfer agreements, especially by PDPs. However, the industrial and technological capacity of the Institutes is still limited and lacks investments, which hinders technological accumulation and diffusion. Thus, improvements are necessary so that the innovation strategies for the SUS present more effective results and can be reversed to the welfare of society.

KEYWORDS National science, technology and innovation policy. Access to health technology. CEIS. Public-private partnerships.

RESUMO *O artigo objetivou apresentar informações relevantes e originais sobre as estratégias de inovação utilizadas por Laboratórios Farmacêuticos Oficiais (LFO) para redução das vulnerabilidades do Sistema Único de Saúde (SUS) e capacitação produtiva e tecnológica do Complexo Econômico-Industrial da Saúde. Como métodos, foram utilizadas a revisão da literatura e a análise de dados primários oriundos de entrevistas realizadas em dois dos maiores LFO do País. Foram identificados e analisados os seus esforços e resultados em Pesquisa e Desenvolvimento (P&D) assim como a incorporação de tecnologias de medicamentos e vacinas, com destaque para as Parcerias para Desenvolvimento Produtivo (PDP). Conclui-se que, apesar de as atividades de P&D ainda precisarem avançar, benefícios foram trazidos pelos acordos de transferência de tecnologia, especialmente pelas PDP. No entanto, a capacidade industrial e tecnológica dos Institutos ainda é limitada e carente de investimentos, dificultando a acumulação e a difusão tecnológica. Dessa forma, melhorias são necessárias para que as estratégias de inovação para o SUS apresentem resultados mais efetivos e possam ser revertidos para o bem-estar da sociedade.*

PALAVRAS-CHAVE *Política nacional de ciência, tecnologia e inovação. Acesso à tecnologia em saúde. Ceis. Parcerias público-privadas.*

[1] Fundação Oswaldo Cruz (Fiocruz) – Rio de Janeiro (RJ), Brasil.
daniela.fernandes@fiocruz.br

[2] Fundação Oswaldo Cruz (Fiocruz), Escola Nacional de Saúde Pública Sergio Arouca (Ensp) – Rio de Janeiro (RJ), Brasil.

Introduction

The partnership strategy between the State and the private sector has proven to be an important instrument for the development of various economic and social sectors. Through several types of agreements, innovative technologies are developed, and new knowledge is shared, benefiting the local innovation and production system. In health, knowledge transfers between the scientific and productive spheres are particularly relevant, as they enable the development of products and services to face problems of the Brazilian phytosanitary framework and strengthen the articulations between these areas, constituting an important mechanism for the dynamization of various activities that integrate the Health Economic-Industrial Complex (CEIS)[1].

However, innovation is one of the biggest challenges in Brazil, considering that, like other countries in Latin America and the Caribbean, Brazil has typically low investments in innovation, incipient use of Intellectual Property systems. Also, there is a disconnection between the public and private sectors in the prioritization of Research and Development (R&D) and innovation activities[2]. These vulnerabilities especially affect the pharmaceutical and vaccine industries, which, due to several challenges, especially those brought by the Fourth Technological Revolution and the COVID-19 pandemic, have sought to grow in innovation, which is a fundamental requirement to maintain the competitiveness and long-term sustainability of firms[3,4].

In order to overcome these vulnerabilities and promote the socioeconomic development of the country, in the last two decades, the Brazilian government has composed a relatively broad system to encourage innovation and strengthen the productive base of health, with the highlight being the Innovation Law (Law No. 10973/2004), the Productive Development Policy in 2008 and the new Legal Framework for Science, Technology, and Innovation (ST&I) (Law No. 13243/2016), regulated in 2018 by Decree No. 9283. In a comprehensive and universal health system, the Unified Health System (SUS), although these strategies have insufficiently promoted technological autonomy, they have favored improvements in social access to products and services and have strengthened the pharmaceutical industrial park, particularly that of public pharmaceutical laboratories, also called Official Pharmaceutical Laboratories (LFO)[4].

In this context, the evolution of the open innovation model has been observed in view of the increase in networks and strategic partnerships focused on innovation and production. The open environment, characterized by the interaction between different actors (research institutions, universities, government, and the industry) for the acquisition and transfer of knowledge and technologies, has been fundamental to boost the development of countries distant from the technological frontier such as Brazil[5]. In the SUS, this interaction has been carried out mainly through the agreements for Technology Transfer (TT), especially the Productive Development Partnerships (PDP)[6,7], which have been constituted as an important instrument for industrial, innovation, and public health policies in the country.

Given that all countries that developed and started to compete in better conditions with the most advanced ones associated a strong industry with an endogenous base of knowledge, learning, and innovation[8], this study sought to analyze the efforts in innovation that have been adopted within the scope of CEIS, by identifying models, mechanisms, interests, and challenges for carrying out technological transfers between public and private institutions.

We sought to bring relevant information to the academic field and contribute to the development or improvement of policies and standards, by providing evidence and suggestions, to encourage the strengthening of productive capacity and national technological learning, which are important to overcome underdevelopment and vulnerability in Brazil[9,10]. In the

literature, studies indicate that there is still a gap in the knowledge of how supplying and receiving companies select transfer mechanisms, as well as of strategies for knowledge acquisition and their impacts on innovation results[11-13].

The article was based on a case study conducted in two of the largest public pharmaceutical laboratories in the country, the Institute of Immunobiological Technology (Bio-Manguinhos) and the Institute of Pharmaceutical Technology (Farmanguinhos), both belonging to the Oswaldo Cruz Foundation (FIOCRUZ). According to the latest information provided by the Secretariat of Science, Technology, Innovation and Strategic Inputs (SCTIE), dated March 2023[14], the Institutes studied have the highest number of PDPs in force, representing approximately 38% of the total medicine and vaccine partnerships of the Ministry of Health (MS)[15]. Thus, they can contribute significantly to understanding the innovation strategies that have been used to reduce the external technological dependence of SUS and strengthening CEIS.

Material and methods

This is a descriptive and exploratory research of qualitative and quantitative nature. Literature review and the analysis of primary data from interviews conducted in two relevant public pharmaceutical laboratories in the period of February and March 2022 were used as the method.

The study was divided into two stages. The first one consisted of a bibliographic and documentary analysis related to the scenario involving TT in the health area in Brazil. Institutional repositories, scientific databases SciELO, Virtual Health Library (VHL), and the CAPES Journal Portal were consulted by searching for the keywords "Technology Transfer" AND Innovation OR agreements and "Productive Development Partnerships" OR PDP, in Portuguese, with social policies or public health as the main subject. The journals best aligned with the study's objective were selected. Institutional documents of public access were also consulted on official websites, such as the Brazilian Association of the Fine Chemistry, Biotechnology and its Specialties Industries, Institute of Applied Economic Research (IPEA), the National Institute of Industrial Property (INPI), the Ministry of Health, the Industry Portal and the LFOs investigated, as well as technical standards, decrees, ordinances, laws, and policies.

In the second stage, field research was carried out. Through a script of semi-structured interviews, 12 in-depth interviews were conducted with the main actors involved in the technology transfer processes of the institutes studied. The interview aimed to identify characteristics of LFO in relation to innovation processes and TT agreements, seeking to portray the current reality and meet present and future expectations.

The roadmap was divided into five blocks, as described below (*table 1*):

Table 1. Roadmap Blocks

Block	Topic	Topics Covered
1	The characteristics of the interviewee	Position and years of experience in the role
2	Characteristics of the Institution in relation to innovation	Number and type of partnerships undertaken, patents, innovative products, strengths, and weaknesses for partnerships
3	Impacts of PDP for LFO and SUS	Technological training, billing, production, human resources, new technological niches, new products generated
4	Partnerships	Mechanisms for prospecting and selecting partners, technologies of interest, priority products for partnerships.
5	Challenges, suggestions, and perspectives	PDP Challenges, PDP Framework, ST&I Legal Framework

Source: Prepared by the authors.

The research project was submitted to and approved by the Research Ethics Committees (CEP) of the Sergio Arouca National School of Public Health (ENSP), National Infectious Diseases Institute (INI) and Oswaldo Cruz Institute (IOC), according to consolidated opinions 5,187,701, 5,202,986, and 5,209,543.

Results and discussion

Technology transfer – concept and challenges in Brazil

There are several concepts available in the literature for technology. According to Dosi[16], the technology encompasses practical and theoretical knowledge and aims at survival in the competitive market, through the search for new combinations-processes and/or products. This set of knowledge involves everything from procedures, methods, 'experiences and know-how to mechanisms and equipment, institutional arrangements, among others'.

The TT concept can be understood as knowledge transfer – the results of technology research and development – to business activity through partnerships between universities, public laboratories, and companies, in an open innovation model[7]. In this sense, the International Technology Transfer (ITT) occurs when the technical knowledge existing in one country is communicated to another, either freely or through a commercial transaction[12]. Among other things, ITT translates into an opportunity to enable developing countries to access state-of-the-art technology without having to invest large sums of resources for their generation.

There are TT mechanisms, from the most original ones, carried out through research on novelties from universities to the private sector, to transfers encouraged to address technological deficiencies in developing countries, such as agreements between private and public companies, which enable continued development for future innovations[17].

As technology is historically concentrated on the most developed countries, not being freely and randomly distributed around the world, much of it is marketed based on Industrial Property Rights (IPR), which, according to several authors, offer strong protection to foreign technology at the expense of local technology, increasing the cost of the former[18].

The concept of TT in Brazil began to gain strength in the 1960s and 1970s, while implementing the development model to substitute for imports. During this period, the Central Bank of Brazil began to analyze, based on the Foreign Capital Law (Law No. 4131/1962), requests for payment of royalties

and technical assistance in foreign currency. For the first time, this law established the obligation to register TT contracts in Brazil and limits were set on royalty remittances, also stipulating that TT contracts should be registered with the Superintendence of Money and Credit (Sumoc). Government intervention in the import of technology, however, basically covered the fiscal and exchange rate issues arising from this trade, and TT is not yet considered a relevant instrument of industrial and technological policy[12,19].

In the early 1970s, with the creation of INPI, which began to regulate and have specific attributions in the TT area, this intervention intensified, providing greater stimulus to local R&D and the assimilation and adaptation of the foreign technology hired. However, with the economic opening that occurred in the early 1990s, INPI's regulatory and supervisory activities were gradually weakened, in line with the reasoning of minimizing state action[12,19].

In addition to the weakening of the regulatory policies related to TT, there is the process of deindustrialization that Brazil has faced since the 1980s, which generated the disarticulation of several productive and innovative systems[20].

Given this scenario, evidence points out that, as seen in the country in recent decades, this process has not collaborated significantly to consolidate an industrialization process that would boost technological learning by local companies nor has fostered the maturation/development of the National Innovation System (SNI)[21]. One of the causes is the reduced degree of internationalization of Brazilian companies, which were not able to absorb external technology and adapt them to the local context, causing an increasing volume of *royalty* payments for foreign technology, verified both by the deficit in the Intellectual Property Balance (BPI) and the deficit presented by the Technological Balance of Payments (BPTec)[12].

According to several authors, growth and economic development are directly related to the incorporation of ST&I in their production processes, in addition to the constitution of a well-structured and effective SI, which depends both on the performance of companies and teaching and research organizations and on the interaction between them and with several other actors, through various types of cooperation[20,22,23]. In this environment, the TT between university, government, and productive sector is pointed out as an alternative and complementary path for the country to reach a higher technological level, being considered one of the best ways to induce partnerships[6].

In Brazil, despite the resumption in the last two decades of an agenda of industrial and ST&I policies aimed at stimulating the scientific and productive sector, with CEIS as one of its priority focuses, the country has faced increasing restrictions in terms of financing scientific and technological infrastructure[24]. According to a study conducted by De Negri[25], federal investments in Science and Technology (S&T) declined about 37% in the period between 2013 and 2020, with a reduction in the innovation rate from 36% to 33.6% in the 2015-2017 period when compared to the previous period (2012-2014), which demonstrates the national challenge for the continuous development of science and innovation in strategic areas such as health.

Transfer of technology in the health area in Brazil

In the Brazilian health area, the transfer of knowledge and technology has been mainly through Technological Cooperation Agreements (TCA) or PDP[7]. These partnerships can strengthen innovative training in the productive sector due to the accumulation of training with a level of excellence in scientific areas in health in Brazil, provided that the actions are articulated for the development of new products and processes[1].

The PDP program, the main instrument for innovation used by the MS, began in 2009, recommending TT agreements and knowledge developed in the private sector for the public, that is, for an LFO. The design of the PDP encompasses not only the manufacture of the finished product but also the internalization of the production of the Active Pharmaceutical Ingredient (API), aiming at self-sufficiency in strategic inputs for Brazil[26]. Therefore, the model has an LFO as a protagonist, which may or may not be associated with other public laboratories or private companies for the production of a certain stage of the manufacture of medicine.

Recent research demonstrates the benefits brought by these partnerships, having as highlights, among others, the proven economy in the purchase of medicines, the expansion of the number of medicines offered to the population[15,27], and the technological learning achieved by national pharmaceutical and pharmacochemical laboratories, with the internalization of various synthetic and biological products and medicines. These results can be translated into numbers, since, according to the information disclosed by the Ministry of Health in March 2023, 68 PDP agreements were in force, involving the transfer of technology and production of 50 medicines, 4 vaccines, and 3 health products, which demonstrates the great participation of PDPs to increase the infrastructure and technological capacity of CEIS[14].

In 2017, through the National Policy for Technological Innovation in Health (PNITS), established by Decree No. 9245, the federal government established two new strategic instruments, in addition to the PDP, to promote the technological training of public administration and private entities in the health area: Technological Orders in the Health Area (ETECS), to be used in the development of solutions that do not exist in the market yet, such as a new medicine or a new form of treatment, or situations of greater technological risk to offer therapies that no longer have national production; and Health Compensation Measures (MECS), to regulate large volume purchases that have little competition.

The establishment of these two new categories of TT was aimed at covering existing gaps in previous legislation. Since its inception, the PDP have turned to the development of existing specific medicines, but whose technology was not yet nationally dominated. The new instruments, both ETECS and MECS, allow the expansion of the scope of partnerships[28]. Detailed information on the strategic instruments, indicating differences between them, is shown in *table 2*.

Table 2. Characteristics of strategic instruments of PNITS

Strategic Instrument	Description	Technology	Partner Selection (via)	TTT	Regulatory policy
PDP	"Partnerships between public institutions and private entities aimed at accessing priority technologies, reducing the vulnerability of the Unified Health System (SUS) in the long term and rationalizing and reducing prices of strategic health products, with the commitment to internalize and develop new strategic technologies and high added value."	Existing but not nationally dominated	Bidding Waiver	Yes	Ordinance No. 2531/2014
ETECS	"Hiring modalities, by the government, of a non-profit research institution, with exemption from bidding, for innovation activities involving technological risk, for solving a specific technical problem or obtaining an innovative product, service or process."	Non-existing, presence of technological risk	Bidding Waiver	Yes or No	Decree 9283/2018
MECS	"Any compensatory practice established as a condition for the strengthening of the production of goods, technological development or the provision of services, with the intention of generating benefits of an industrial, technological or commercial nature achieved."	Existing	Licitation	Yes or No	*

Source: Prepared by the authors based on Law No. 8666/1993[29], Ordinance No. 837/2012[30], Decree No. 9238/2018[31].

*There is still no regulation by specific legislation.

Regardless of the model, the important thing is that the interests of the country or of the institution that is hiring are covered in the instrument, and they should be responsible for selecting the technology to be transferred and choosing the operational model of the transfer.

Interview results

Five key actors from Bio-Manguinhos and seven from Farmanguinhos participated in the research. The interviewees had an average experience of ten years, and the roles informed covered strategic areas of TT agreements, linked to prospecting, negotiation, advising, selection, and project management. The profile identified in block 1 demonstrates the great involvement of respondents with the agreements and the broad knowledge about the challenges and strategies in innovation for SUS, bringing reliability to the information and evidence collected.

Block 2 sought to identify innovation efforts, more specifically in relation to R&D, Intellectual Property, and TT agreements. The participants were found to carry out internal and external R&D activities in universities and private companies and they have an Internal Innovation Center (NIT), which already demonstrates the alignment with the Innovation Law (Law No. 10973/2004) and with the Innovation Policy of FIOCRUZ, a scientific institution to which they belong. The initiatives also express the commitment of these LFO to creating a pro-innovation environment aimed at strengthening endogenous development and TT cooperation.

Regarding patents, Bio-Manguinhos reported having 38 patents granted and 2 patents filed. Farmanguinhos had 7 patents granted

and 7 patents filed. The products with granted patents include:

I) Bio-Manguinhos – Meningitis C conjugate vaccine, flavivirus DNA constructs, anti-MRSA antibody, dengue DNA vaccine, artificial calibration virus (NATkit) and anti-Leishmania antigens;

II) Farmanguinhos – bioinsecticide composition, the process for Obtaining Dry Steroid-Derived Ergostane, diphenyloxyalkylamine derivatives, α-ketoacyl compounds of isoniazid, pharmaceutical composition, use of fixed-dose mefloquine, compounds derived from phenylamino-pyrimidine, compounds derived from isatin.

As innovative initiatives, the development of some original products (disruptive innovations) was informed. Bio-Manguinhos cited the meningococcal conjugate C vaccine, the double viral vaccine (measles and rubella) and diagnostic kits, including the SARS-CoV-2 molecular kit for COVID-19. Farmanguinhos reported having developed the Biological Larvicide Dengue tech.

Despite the commitment shown in the generation of R&D, its innovation results show that there is still a way to go until they become a reference in S&T. One of the explanations for this refers to their origins, since they did not have their creation associated with the development of innovations, but with the production of topical medicines, antipersonnel serums and vaccines to combat epidemics, resulting in low participation in the National Health Innovation System (SNIS) when compared to universities, research institutions, and the private market[32,33].

Table 3 summarizes the types of cooperation agreements used by the institutions. Ongoing PDPs and agreements signed in 2021 were considered, except for those under negotiation.

Table 3. Ongoing agreements in Bio-Manguinhos and Farmanguinhos

Type of agreement	BIO	FAR
Product Development Partnership	13	13
Non-Disclosure Agreements	31	34
Agreements for the transfer of biological material	1	1
Research and Development Agreements (including agreements for clinical trials)	4	2
Technology Transfer Agreements	2	5
Technical Cooperation Agreement	7	5
Agreements for the provision of technological services	1	6
Technological Order	1	0

Source: Prepared by the authors.

In addition, the following were cited by Bio-Manguinhos: two Revenue Agreements, an International Partnership Agreement, three Cooperation Agreements without resource transfer, a co-development Agreement, know-how transfer Agreement, and four Partnership Agreements based on the Innovation Law. And the following by Farmanguinhos: an international partnership agreement in ST&I.

As expected, many agreements were cited, corroborating the open innovation strategy that has been followed by the public and private pharmaceutical industry. Highlight can be given to PDPs, which are in various stages of evolution, and to the considerable number of Confidentiality agreements. These agreements, also known as NDAs (Non-Disclosure Agreements), are generally concluded before closing the project or ending the partnership, still in the stage of talks between stakeholders. The objective is to protect, from the first exchanges of intentions, the information shared between the partners, to later define the best instrument, according to the progress of the negotiations.

When asked what leads other companies to seek partnerships with the LFO, the interviewees selected in order of relevance: access to SUS demand, technical knowledge, tradition in the production of medicines or vaccines, tradition in R&D, good manufacturing practices and good Image/reputation (linked to FIOCRUZ). On the other hand, the most selected factors that removed the interest of private partners were: insufficient investment in infrastructure, lack of agility in responding to demands, lack of an entrepreneurial culture, and insufficient human resources.

The access to SUS demand, the most cited strength, has a high relationship with the LFO's own link with the MS, which supposedly facilitates negotiation, and with the PDP program, which offers the technology holder exclusivity in the purchase of the product for the period in which the TT lasts, to stimulate the interest of companies in the market. This acquisition model can be negotiated by the LFO with the MS for other types of agreements, provided that the product is considered essential or strategic for the SUS and has centralized acquisition.

As for the insufficient investment in infrastructure for innovation, a factor considered more fragile by the interviewees, there is compliance with the characteristic of developing countries. The social problems of these countries, such as the lack of access to quality education, health care, and various basic public services, lead their governments to consider science, technology, and innovation as secondary issues[2].

Block 3 aimed to investigate the impact of PDPs for LFO. Respondents answered that, by bringing new products and projects, these partnerships increased revenue, human resources, and production volume. According to Farmanguinhos' managers, there was an increase in volume and revenue of more than 200%.

When asked if the PDP portfolio has allowed or will allow the LFO to operate in new productive niches, the response was positive. Both Bio-Manguinhos and Farmanguinhos reported that, through the PDP, it was possible to act in new therapeutic classes, which enabled the incorporation of productive areas, such as biological medicine for chronic diseases, rare diseases, and cancer (Bio) and immunosuppressive and anti-Parkinsonian drugs (Far), as well as those that have projects for the construction of areas for new therapeutic indications.

They also stated that the acquisition of knowledge of innovative technologies for LFO has provided studies for the generation of new products and expanded their technological capacity. A recent example, cited by a Bio-Manguinhos interviewee, was the production of the COVID-19 vaccine, the result of a technological order from the pharmaceutical company AstraZeneca and the University of Oxford. The fact that Bio-Manguinhos already has accumulated knowledge in biopharmaceuticals, in addition to an infrastructure with state-of-the-art technology, due to PDP investments, allowed the TT to be completed quickly, and the product could be fully manufactured in Brazil.

Block 4 focused on the mechanisms for prospecting and hiring partnerships. The interviewees selected the consultation of Intellectual Property bases, the consultation of international supplier platforms, the visit

to technology fairs, and the evaluation of company portfolios as mechanisms used for prospecting. For the selection, public calls and direct contact with the company holding the technology were indicated, which is the predominant model, since the products are mostly protected by patents or produced by a single supplier.

There is an addendum to the selection of the partner. This is a very controversial topic, and the fact that it is a hypothesis of bidding exemption, as listed in article 24, item XXXII of Law No. 8666/1993, does not rule out the need for prior objective and transparent procedures by public managers. To regularize this situation and bring more transparency to the hiring process, the Federal Court of Auditors (TCU), through Appellate Decision No. 1730/2017, determined that public laboratories carry out a selection or pre-qualification process when choosing the private entity, using the public calls as a model. This model should therefore be used in the following cases: selection of partners for joint development of a product, non-exclusive manufacturer of the intended product, products without patent or with expired patent.

Therefore, apart from cases of unenforceability of bidding, the public bids is the model that must be adopted, which has already been used by some LFO, such as Farmanguinhos. The public bids, in the eyes of publicity, legality and morality, represents an evolution since it brings standardization to hiring by LFO and compliance with constitutional principles.

As for the technology to be transferred, there was greater interest in partnerships that bring innovative technologies to the country and in collaborative research, already the result of the stimulus brought by the new Legal Framework for Innovation. Despite the reported interest, technological orders, aimed at non-existent products in the market, are still little used, and, at the moment, only one is in execution, carried out by Bio-Manguinhos, as already mentioned.

Regarding the profile of the partners, the LFO reported having greater interest in the interaction, in order of preference, with private companies, other public laboratories, and national and international universities. No partnerships with non-governmental organizations and startups were identified as a priority. In relation to this issue, the low interest in hiring startups is noteworthy because they are organizations designed to create new products or services in conditions of extreme uncertainty[34,35] and can thus contribute to identifying and solving market gaps, as well as to bringing researchers closer to the culture of entrepreneurship, necessary for more products to leave the stands and be made available in the public market.

Regarding the priority products establishing partnerships, the three most indicated were, in order of number of citations: neglected product or with potential risk of shortage, with high acquisition value for SUS, and with alignment with its technological plants. As for medications for neglected diseases, despite the mentioned priority, what has been observed in practice is that few agreements have been made for the production and TT of this class of medication, with few exceptions[36]. According to some interviewees, this is due to the lack of a state policy that prioritizes these low-cost medicines, enabling strategies for the supply of APIs and making public production economically viable.

Block 5 aimed to identify challenges, collect suggestions and opinions on the PDP model and on the legislation involving TT agreements, aiming at their improvement.

As internal and external challenges for carrying out TT agreements, these were identified by the interviewees in order of number of citations (*table 4*).

Table 4. Internal and external challenges for the implementation of TT agreements

Internal challenges	External challenges
– agility in responding to demands; – collaboration and interaction between the sectors involved; – alignment with the partner; – bureaucracy of public administration; – lack of team dedicated to the projects; – lack of resources for reinvestment in the project; – insufficient number of personnel; – hardening of management processes; – current management model; – planning based on the lack of definition and clarity on the end of the MS regarding demand and prices; – competition with the market and the need to expand knowledge about the possibilities of the Innovation Law.	– lack of investment to adapt the manufacturing infrastructure; – often insufficient budget to cover expenses; – time/transfer ratio and absorption of knowledge or technologies that are the object of the partnership; – legal uncertainty (need for changes in the legal framework); – political instability; change of actors in government; – insecurity regarding the maintenance of the price and volume of acquisition by the MS; – exchange rate fluctuation; – international logistics; – pressure from the control bodies; – difficulty for foreign partners to adapt to Brazilian legislation; – culture of external public agents in relation to the need for investments in Research, Development and Innovation (RD&I).

Source: Prepared by the authors.

Regarding the PDP, some improvements were pointed out by the interviewees, and the most prominent ones were: I) Platform orientation (would reduce competition between the LFO themselves); II) Evaluation and monitoring of the investment necessary to complete the TT during the period of the agreement (this did not happen); III) Market analysis for the calculation of costs and risks involved in the partnership; and IV) Specific law for PDP, due to the differentiated model of these agreements (acquisition linked to TT). Thus, hiring would not have to comply with Law No. 8666/1993, facilitating the evaluation of control bodies.

With regard to the expectation about the future of the PDPs, the unanimous response is that there is a lack of political will to move forward. According to the interviewees, something that should be rethought by the Ministry of Health and the control bodies is the view of the lowest price, which does not consider the strategic character of the PDPs nor their difference in the medium and long term for the country in the face of a common acquisition, which neither generates knowledge, nor jobs for Brazil. The PDP policy, in turn, was cited as of great relevance to develop the medicine production chain and to reduce the trade balance deficit, in addition to presenting economic advantage over other types of agreements, according to some interviewees.

However, there has been no announcement of a new list of strategic products since the change of government in 2017, and the current scenario of uncertainty, combined with the lack of clarity on some topics of the PDP Legal Framework (Ordinance No. 2531/2014) and the new incentives of the Innovation Law (Law No. 13243/2016), has led LFO to seek new types of agreements.

The interviewees understand that improvements are necessary for the regulatory framework of the PDP, regulated by Consolidation Ordinance No. 5/2017 (Annex XCV), according to the suggestions presented in *table 5*.

Table 5. Suggestions for improving the PDP Legal Framework – February 2022

Suggestions for improving the Framework (Ordinance No. 2531/2014) through the review of the PDP regulations (Ordinance No. 05/2017 – Annex XCV)	
Bio-Manguinhos	**Farmanguinhos**
– distinction of the concept and responsibilities of the private entity that owns the technology, the private entity that develops/absorbs the technology;	– better definition of RD&I and PDP;
	– better clarification on Phase IV and its closure;
– characterization and distinction of API concepts of synthetic API products from organic products;	– clarification on the nationalization of the national API and its acquisition after the finalization of the PDP by the LFO;
– alignment of concepts between the product object of PDP and the API;	– approval of the demand for 100% of a medicine for only one laboratory (to analyze the division of demand, as it impacts the viability of the project);
– adaptation of the text to the reality of PDPs of organic products;	– definition of clear criteria to differentiate the values of medicine acquisition and technology transfer;
– greater clarity should be given at other parts in the text.	– minimum criteria for the composition of monitoring reports;
	– criteria and indicators for assessing technology transfer.

Source: Prepared by the authors.

With regard to the opportunities brought by the new ST&I legal framework (Law No. 13243/2016) and its updates, interviewees considered that they will bring modernization, requiring the control bodies to align with the new model, which may not be in convergence with public procurement legislation. The interviewees also informed that they are studying all the possibilities that the law offers, and they have teams dedicated to this. However, they have already mentioned positive contributions brought by the law, such as the stimulation of cooperation and interaction between the LFO and the private sector, the possibility of providing specialized technical services to third parties in activities aimed at research and innovation; the constitution of NITs with their own legal personality, the hiring of research abroad, the opportunity for joint development, the possibility of treating innovation separately from production, the sharing of laboratories and infrastructure with third parties, either through financial counterpart or not.

Conclusions

This article showed that the interaction between government-enterprises-universities, through partnerships, has been fundamental to expand the learning process of the public pharmaceutical industry, although it is not an easy path to be followed. There are many barriers in this relationship, such as the difference in the actors' purposes, bureaucracy in the formalization of contracts and political, legal, and commercial instability.

From the results of the study, however, it was possible to know mechanisms and innovation strategies used by public pharmaceutical institutions to reduce the vulnerabilities of the SUS, as well as the benefits brought by the TT agreements, especially by the PDPs,

which are concrete and innovative instruments of the use of the purchasing power of the State for the transformation in the productive health system. The answers of the interviewees, people involved in the daily life of the PDPs, are in line with this statement. Despite the challenges reported, they consider that there has been a growth in the training of their professionals and expansion of their manufacturing infrastructures, which has contributed to the diversification of portfolios and the generation of jobs, essential factors for the expansion of access to health and development in the country. Despite the reported benefits, the evidence of the study demonstrates that R&D activities need to advance and that the industrial and technological capacity of LFOs is still limited and lacks investments, which hinders their strategies in technological accumulation and diffusion.

Thus, changes of governmental and institutional order are seen as urgent, so that the innovation strategies for the SUS present more effective results and can be reverted to the well-being of society, including: change of culture on the part of the Ministry of Health, which must act not only in the monitoring and collection of results, but also as a guiding agent and facilitator of the activities of the LFO in institutions such as INPI, the National Health Surveillance Agency (ANVISA), and the control bodies; changes in the Legal Framework of the PDP, according to the suggestions presented, aiming at improvement; expansion of investments in R&D infrastructure by the MS and search for new sources of resources, investments and partnerships by the LFO; expansion of knowledge and use of opportunities brought by the Legal Framework for Innovation by the LFO; greater use of other strategic instruments established by PNITS, in addition to the PDP (technological order and MECS), aiming at agreements not only for TT already dominated, but, above all, for local development projects of original technologies or acquisitions more beneficial to the country; the reestablishment of PDPs, with the dissemination of a new list of strategic products, in which the balance between the health and economic issue prevails; the implementation of a policy targeted at neglected medicines, aiming at the viability of production and development of national research for this type of medicine; a greater interaction of the industry with the area of care services, given that this relationship is an important indicator for paths and priorities of the SUS for investment, among others.

Finally, it is understood that the article has provided answers to some knowledge gaps, giving visibility to the topic and adding important contributions to projects aimed at innovation in medicines and vaccines for SUS. The results also demonstrate the essential character of maintaining strategic policies and programs that privilege health, science, technology and innovation, given the vulnerability of the country and the health needs of the Brazilian population.

Collaborators

Fernandes DRA (0000-0002-0969-2707)* contributed to the design, planning, data collection, interpretation of results, and writing of the work. Gadelha CAG (0000-0002-9148-8819)* contributed to the supervision of the study, analysis, and critical review of the manuscript. Maldonado JMSV (0000-0002-0815-1765)* contributed to the analysis and critical review of the manuscript. ■

*Orcid (Open Researcher and Contributor ID).

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