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Technical review by
**Dr. Julia Paranhos**,
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# INNOVATION AS A PUBLIC STRATEGY

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# PRESENTATION

This article is the result of a project developed by Idec, *Instituto Brasileiro de Defesa do Consumidor* (Brazilian Institute for Consumer Defense), in partnership with the Open Society Foundations on innovation policies and production of medicines and vaccines in the context of Covid-19. Idec is a civil society organization that strives for fair consumption, and whose mission is to contribute so that all citizens have access to goods and services that are essential for social development, sustainable consumption, the health of the planet, and the consolidation of Brazilian democracy.

In carrying out its activities, Idec adopts a broad concept of consumer: more than the individual who exercises their purchasing power in the consumer market, it is everyone who potentially has or should have access to essential products and services[1]. In the specific case of health, Idec strives for access to quality services, understanding that the most sustainable and equitable way to achieve this goal is through universal access systems, such as SUS, *Sistema Único de Saúde* (Unified Health System).

Idec believes that, even within the scope of the private market for health products and services, the state can be a great catalyst for distributive results and productive efficiency. Through its regulatory role, the state organizes markets, establishes rules that guarantee legal certainty and distributes responsibilities among economic agents. In the case of the pharmaceutical market and pharmaceutical assistance policies, it is no different. The state regulates R&D&I (Research, Development and Innovation) policies, guarantees quality standards through Anvisa, *Agência Nacional de Vigilância Sanitária* (National Health Surveillance Agency), limits prices and even produces medicines and vaccines that the market has no interest in providing.

The Covid-19 pandemic has imposed on health systems, universities and the pharmaceutical industry the unprecedented chal-

1. This broad concept involves users of essential services and people excluded from the consumer market due to lack of purchasing power. SODRÉ, Marcelo Gomes. "Agências Reguladoras e a Tutela do consumidor". *Série Pensando o Direito*, nº 21/2010. Brasília: Secretaria de Assuntos Legislativos, 2010, p. 6.

lenge of offering innovative solutions in health technologies in record time to face the new disease.

Thus, when the negotiation processes for the procurement and transfer of technology in Brazil began in 2020, the importance of these processes to guarantee the right to health and life, and even the relevance of recording the experiences of vaccine development and production, became evident to Idec.

The right to be immunized against Covid-19 (and access to this essential service) is closely related to a series of connected public policies that range from the regulation of clinical trials, the promotion of R&D&I, patent rules, infrastructure, guarantee of productive capacity (public and private), to international agreements and the use of centralized procurement to negotiate better prices. There is a long road between the scientist who develops the vaccine and the nurse who applies it in the health service, as well as complex networks of actors that can and should be evidenced and recognized.

The novelty of Covid-19 posed additional challenges to these arrangements, especially regarding the urgency of a sanitary solution and the mitigation of uncertainties involved in the process of developing new technologies to prevent and cure the new disease. That is why it is so important to record these experiences and share them internationally, which is the main objective of this publication.

In the spirit of sharing, this document, prepared by a civil society organization, is aimed at disseminate the knowledge acquired in this process, in addition to future analyses that will follow both in the academic and political fields[2].

2. The Brazilian immunization process had the active participation of several non-governmental organizations in claiming health priorities and vulnerability in vaccination, transparency in the distribution process, and expansion of competing producers through the compulsory licensing of technologies related to Covid-19.

# INTRODUCTION

The Covid-19 pandemic has imposed the need to develop an urgent public health solution to a problem of high public interest. In addition to measures to stop infection, such as physical distancing and the mandatory use of masks, the development of vaccines, drugs and treatments has become central. Moreover, institutions and companies have allocated various resources to make vaccines and pharmaceuticals viable in the shortest possible time to treat the Sars-CoV-2 virus[3].

The first months of this process comprised a global race for vaccines, in which management and investment in innovation and negotiation for technology transfer represented differentiators of impact. Several networks, formed by universities, research institutes and pharmaceutical companies, began to organize themselves into complex arrangements having an international outreach. The intention was to coordinate their efforts to develop a faster and safer innovative solution against the unprecedented infection.

Brazil followed the same path, although with significant differences related to the installed public laboratory infrastructure, consolidated experience in vaccine production for the PNI (National Immunization Program), and a universal access system with a tradition of using their purchasing power to guide public production. Such factors played a crucial role in Brazilian productive autonomy and, consequently, in guaranteeing vaccines for the population. This was an experience whose records and further studies can guide other countries, especially middle- and low-income ones, in facing health crises.

3. Since the recognition of the pandemic status by WHO (World Health Organization) in March 2020, in the first six months of the pandemic alone, 44 million cases of infection with the new coronavirus were identified and more than 1.2 million people lost their lives due to the illness. Available at <*glo.bo/3ARnNZW*>, accessed November 20, 2021.

Specifically in Brazil, in the same period there were more than 154 thousand deaths, with more than 5.2 million infected. Available at <*glo.bo/3Gi4oT3*>, accessed on November 20, 2021.

With that in mind, the present article seeks to present the Brazilian case of technology transfer and local production of CoronaVac (initially registered worldwide by the Chinese company Sinovac) and AZD1222 (initially registered worldwide by the european company AstraZeneca and also known as Oxford vaccine) vaccines. This article also highlights the peculiarities of the legal panorama of science and technology promotion, industrial policy and health policies that resulted in a rapid advance of the national vaccination campaign, compared to other middle-income countries[4].

Therefore, the following topics will present the panorama of Brazilian public laboratories and their relevance and relationship with the centralized purchasing policies of the Ministry of Health. Then, we will address the challenges related to overcoming uncertainties for the development of new health technologies, and the instruments that Brazil has for promoting their mitigation. In addition, the technology transfer processes carried out by the Brazilian public laboratories Fiocruz (Fundação Oswaldo Cruz) and Instituto Butantan will be reported[5]. Finally, the present article will present some conclusions about this process, emphasizing not only its meaning for the fight against Covid-19, but also the relevance of risk assessment and mitigation processes for increasing public investment in new health technologies.

4. In November 2021, more than 314 million doses of vaccine against Covid-19 were applied in Brazil, representing more than 136 million people fully vaccinated, or more than 64% of the population. Available at <bit.ly/3se4giE>. Accessed on November 30, 2021.

5. Methodological note: for this report it was used a descriptive-documentary approach of the legal landscape and contractual instruments related to technology transfers that have been made available to the public. Fiocruz's contract was fully available to the general public, while Butantan's was not. Thus, the research was complemented with public statements given by laboratory representatives at events. This article is essentially descriptive, offering some possible inferences about the Brazilian case of immunization against Covid-19 at its end.

# OFFICIAL PHARMACEUTICAL LABORATORIES AND CENTRALIZED PROCUREMENT

Brazil recognizes health as a right and ensures it to its residents through a health system with universal access (SUS). This system includes the universalization of pharmaceutical care. The Pnaf - *Programa Nacional de Assistência Farmacêutica* (National Pharmaceutical Assistance Program) involves the federal government, states and municipalities, which buy and supply medicines to the population, while the PNI - *Programa Nacional de Imunização* (National Immunization Program) provides vaccines. The Ministry of Health acquires strategic supplies such as medicines or vaccines for diseases of national epidemiological relevance (HIV and syphilis, for example).

The National Immunization Program was created in 1973 and improved since then, especially with the creation of the SUS in 1988. In the 1980 decade, for instance, PNI achieved the immunization of 18 million children in a single day against poliomyelitis, contributing for the region of the Americas becoming the first of the world to be considered free of polio.

The centralized purchasing mechanism presents considerable advantages in terms of gains in scale for the Ministry of Health. For suppliers, the economic impact of a procurement made by the Brazilian Ministry of Health is great, considering its intention to supply the entire Brazilian population, as it also converts this mechanism into an instrument to encourage national industry[6] and technological innovation[7]. The successful combination of public production and centralized purchasing ensures the economic stability of the LFOs on the one hand, and the guaranteed supply of medicines and vaccines at reduced prices by the Ministry of Health, on the other hand.

Historically, effective immunization policies depend on resilient health systems capable of reaching the population, and on the availability of vaccines. In the field of logistics, Brazil is an example of success. In addition to the centralized acquisition of immunizations by the Ministry of Health, the PNI distributes doses through the Primary Health Care structure spread throughout the national territory.

In addition to buying and supplying medicines to the population, SUS also encompasses pharmaceutical production. The public manufacturers are the LFOs, *Laboratórios Farmacêuticos Oficiais* (Official Pharmaceutical Laboratories), agencies that present themselves in different forms of organization and with different portfolios, However, they maintain the common characteristic of being state-owned and of supplying materials to both the public system and to non-commercial programs of international organizations, such as the WHO (World Health Organization) and UNICEF (United Nations International Emergency Fund for Children).

Currently, there are 33 public laboratories formally constituted in Brazil, but only 17 have an active drug registration with the Brazilian drug agency, Anvisa[8]. Their legal form and even their institutional subordination varies greatly: there are LFOs linked to universities, the Armed Forces, state governments and the Ministry of Health. As for their administrative structures, some are university units, others are public foundations, and there is one constituted in the form of a public company. There is, therefore, a great plurality of institutional arrangements[9].

In terms of economic relevance, variety is also the rule. There are inactive laboratories, laboratories that produce low value-added inputs (hand sanitizer, for example), and laboratories that supply high technology products such as vaccines and monoclonal antibodies. In the Brazilian pharmaceutical sector, including private companies with national capital and transnational companies, there are two public producers that are among the twenty producers with the highest revenue in the country[10], Fiocruz and Instituto Butantan. Along with Hemobrás (Brazilian Company of

6. PIMENTEL, Vitor Paiva. "Parcerias para o Desenvolvimento Produtivo de medicamentos no Brasil sob a ótica das compras públicas para inovação: 2009-2017".

7. FOSS, Maria Carolina; et al. "Compras públicas como instrumento de política de inovação orientada à demanda: experiências no Brasil, nos Estados Unidos e na União Europeia", 2019.

8. FIGUEIREDO, Tatiana Aragão; FIALHO NETO, Renato Gonçalves; MAGALHÃES, Jorge Lima de. "A produção pública de medicamentos no Brasil". *Ciência & Saúde Coletiva*, v. 26, pp. 3423-3434, 2021.

9. OLIVEIRA, Egléubia Andrade de; LABRA, Maria Eliana; BERMUDEZ, Jorge. "A produção pública de medicamentos no Brasil: uma visão geral". *Cadernos de Saúde Pública*, v. 22, pp. 2379-2389, 2006.

10. PARANHOS, J.; PERIN, F.; VAZ, M.; FALCÃO, D.; HASENCLEVER, L. Articulação de políticas e instrumentos de produção e inovação para o Complexo Industrial da Saúde no Brasil, 2003-2017: os casos do Inova Saúde e do Profarma. Relatório de pesquisa – convênio UFRJ/IE/OSF Rio de Janeiro: GEI/IE/UFRJ, 2021.

Hemoderivatives), they are the only ones with annual billing of more than R$ 400 million[11].

In terms of supply capacity, LFOs are relevant to the Brazilian health system for two main reasons. First, they produce medicines important to public health that are of little interest to private industry, given their low added value (the final stage of benzathine penicillin, for example)[12] and high-tech medicines with a high price in the private market, relieving the costs of public pharmaceutical assistance[13].

In recent decades, especially between 2008 and 2015, public manufacturers were instruments of various public policies for technology transfer, especially PDPs - *Parcerias de Desenvolvimento Produtivo* (Partnerships for Productive Development). PDPs encompasses a private partner that agrees to transfer technology with the public laboratory and have assured the purchase of their product for a limited period.

Within the setting of public policies for innovation of the pharmaceutical sector, PDPs are the most used tool and have even continued after the shrunk of these policies noticed after 2016[14], despite some suspensions on the partnerships, especially after 2019.

Among the most relevant LFOs are Instituto Butantan, associated with the São Paulo state government, and Farmanguinhos (Institute of Technology in Pharmaceuticals) and Bio-Manguinhos (Institute of Technology in Immunobiologicals), associated with Fiocruz - which is linked[15] to the Ministry of Health, despite having great autonomy and democratic internal governance. Butantan and Fiocruz are centennial Brazilian institutions which, historically, are strongly related with vaccine production. Both were created for this purpose and today have relevant vaccine portfolios.

The Butantan Institute was created in 1901, initially focused on the production of serum to combat the Bubonic Plague that was ravaging the country at the time, but soon transferred its vocation to the manufacture of immunobiologicals. In the 2000s, the Institute celebrated a technology transfer partnership, for the production of the vaccine against Influenza with the transnational company Sanofi, marking an important step in the development of the laboratory's technological capabilities. Currently, Butantan is able to supply the entire Brazilian demand for trivalent influenza vaccine, producing around 140 million doses annually.

The two laboratories were included in the PDPs policy, especially in the biotechnological drugs sector. *Gomes et al* identify how these two units were among the main laboratories to celebrate agreements of this nature for biosimilar production, which amplifies their manufacturing capacity[16].

11. VIEIRA, Fabiola Sulpino; DOS SANTOS, Maria Angelica Borges. "O Setor farmacêutico no Brasil sob as lentes da conta-satélite de saúde". Texto para Discussão, 2020.

12. Furp only produces the final stages of benzathine penicillin, importing the API.

13. CHAVES, G. C.; TAVARES, Noemia Urruth Leão; "Construção da Soberania em Saúde: Política e Produção Pública de Medicamentos no Brasil". *Boletim do Observatório Ibero-Americano de Políticas e Sistemas de Saúde*, Brasília, pp. 1-8, 2014.

14. PARANHOS, Julia; MERCADANTE, Eduardo; HASENCLEVER, Lia. Os esforços inovativos das grandes empresas farmacêuticas no Brasil: o que mudou nas duas últimas décadas?. Revista Brasileira de Inovação, v. 19, 2021.

15. Fiocruz, in fact, is a research foundation linked to the Ministry of Health that has two LFOs Farmanguinhos and Bio-Manguinhos.

16. GOMES, Eduardo Braz Pereira et al. Desenvolvimento de biossimilares no Brasil. Fronteiras: Journal of Social, Technological and Environmental Science, v. 5, n. 1, p. 31-42, 2016.

The extensive national public production of vaccines is related to decades of experience of the Brazilian health system, in ensuring an effective immunization strategy through the PNI, which involves the centralized procurement of vaccines by the Ministry of Health.

The extensive national public production of vaccines is related to decades of accumulation of the Brazilian health system in ensuring an effective immunization strategy through the PNI, which involves acquiring vaccines centrally by the Ministry of Health.

In the Brazilian case, capacity building for the public production of immunizations was addressed with state investment in public policies for local production. In 1985, the Pasni, *Programa de Autossuficiência Nacional em Imunobiológicos* (National Immunobiological Self-Sufficiency Program) was created. It was intended to constitute a public productive park, replace imports, and make public health actions viable through the PNI. Today, the country has public pharmaceutical laboratories capable of supplying the national program and even international programs of the WHO.

According to the consolidation of data from the Association of Official Pharmaceutical Laboratories of Brazil (ALFOB), public laboratories produced 300 million doses of vaccines in 2017 and in 2019 had pharmaceutical registration of 18 of the 26 vaccines included in the National List of Essential Medicines (Rename, in the portuguese acronym)[17].

17. Disponível em: <***bit.ly/3AobndN***>

Bio-Manguinhos at Fiocruz, for example, supplies SUS with different vaccines and has exported its surplus to more than 70 countries. The laboratory has been pre-qualified by the WHO, since 2007, to supply the Meningococcal AC vaccine. It, along with UNICEF, supplies the organization's program, which takes immunizers to more than ten countries on the African continent. Likewise, the Butantan Institute supplies SUS with seven vaccines, including those against Influenza, Hepatitis A, Hepatitis B and Rabies.

The virtuous relationship between centralized purchasing and public laboratories can be seen in other examples, in the aforementioned WHO and UNICEF meningitis program, supplied by Fiocruz, and in Cuba's Finlay Institute. It can also be seen in the case of the antiretroviral drug Efavirenz which, in 2007, was subject to a compulsory license issued by the Brazilian government and produced by another public manufacturer linked to Fiocruz, Farmanguinhos.

In addition to immunization policies and centralized purchasing, it is also necessary to emphasize the role that their combination with Industrial and Science, Technology and Innovation policies had, and still has, for the development of vaccines and for the national pharmaceutical panorama in Brazil

# UNCERTAINTIES AND RISKS OF INNOVATION AND THE IMPORTANCE OF STATE PARTICIPATION

Innovating is a difficult process, with no guarantee of success. This is even more so in radical or disruptive cases, which require long-term investments in basic research. Investing in R&D&I aimed at technological change requires a long wait before new products appear on the market, in addition to the prospect that most developed products fail: that is, they do not give the expected return[18].

Due to these difficulties, which are intrinsic to the innovation process, there is a relative consensus in the literature as to the role of the state. That role is seen as complementarily supplying demands not met by companies; or, creating synergies in specific fields such as infrastructure, R&D&I (Research, Development and Innovation), education, health[19], among others, in order to achieve results that are useful and of priority interest to society.

Some go even further in this analysis, concluding that the return on investment in innovation is so uncertain that the processes of developing new technologies cannot even be understood through rational economic theory[20] and concepts such as market failure. For Mariana Mazzucato, the problem with studying the knowledge economy from an orthodox economic perspective (and the notion of market failure) is that it ignores a fundamental fact about the history of innovation: that governments have not only funded the riskiest research (whether basic or applied), but also were often the source of funds for the most radical types of innovation. "To that extent, [the state] has been actively creating markets, not just correcting them."[21]

In the economic literature, the line of thought that deals with the perspective of a demand-oriented economy sees the state as a source of innovative and disruptive solutions for the construction of a common good. In this line of thought, it is the state that leads the technological trajectories through the elaboration of

18. MAZZUCATO, M. "The entrepreneurial state: debunking public vs. private sector myths. New York: Anthem Press, 2014 p. 77. No mesmo sentido, ver a abordagem de sistemas em O'CONNOR, G.C. "Major innovation as a dynamic capability: A systems approach". *Journal of Product Innovation Management*, 2008, 25(4): 3131-30.

19. TIROLE, J. *Economia do bem comum*. 1a ed., Rio de Janeiro: Zahar, 2020.

20. Idem, p. 78

21. MAZZUCATO, M. The entrepreneurial state: debunking public vs. private sector myths. New York: Anthem Press, 2014. p. 80-1

public policies to encourage innovation aimed at meeting society's critical needs (demand); and, provides solutions that the companies, by themselves, could not provide, given the high degree of uncertainty of the return on investment.

The case of the pharmaceutical market is exemplary. It is known for its intensive use and promulgation of technology, and it has its own ecosystem of actors, including large transnational companies, small biotech companies, public laboratories, governments and even universities. And, although this is an innovative market with considerable private funding, recent studies have shown that the most productive investments, which result in truly innovative medicines, are those derived from public sources[22].

22. According to Mazzucato, of the 1,072 drugs approved by the FDA (Food and Drug Administration) between 1993 and 2004, only 357 were New Molecular Entities and not just variations of existing drugs, also called "*me too*". The number of new "priority" drugs (New Molecular Entities rated 'P') really important for health is even more worrisome: only 146 of them had this rating. In: MAZZUCATO, M. The entrepreneurial state: debunking public vs. private sector myths. New York: Anthem Press, 2014, p. 84.

To understand this process, and how the Brazilian legal landscape has or has not embraced these theories, it is important to analyze some key concepts for understanding R&D&I policies. For situations in which we deal with the need to develop an unprecedented technological solution, it is necessary to proceed with (i) technological prospecting, (ii) assessment of the stage or technological maturity of a given solution, and (iii) assessment of the risk and uncertainty involved in the process of developing the new solution or trajectory.

Prospecting is the activity of researching technologies already partially or fully developed that could be used in the development of a new trajectory or technological route. Technological maturity, on the other hand, corresponds to the maturity level to which a given process or technology has developed, in relation to the others available at that time. Finally, assessment of technological risk involves how accurately it is possible to measure the probabilities of future events that affect the execution of innovation projects; whereas assessment of technological uncertainty involves situations in which, initially, it is not possible to obtain all the information necessary for the calculation of probabilities about the occurrence of future events that may influence the trajectory of technological development[23].

23. Mariana Mazzucato, in "O Estado Empreendedor", presents the differentiations between risk and uncertainty made by Knight and Keynes, both based on the level of knowledge one has about the possible results of the enterprise. MAZZUCATO, M. The entrepreneurial state: debunking public vs. private sector myths. New York: Anthem Press, 2014.

It is the assessment of risk and uncertainty that makes it possible to define the skills and infrastructure necessary to develop a technology to the stage where it can reach the market. Such assessment also provides the criteria to determine which instrument will be selected to enable this development, the contracted object, the budget profile and the remuneration modalities.

The assessment of technological risk or uncertainty can be made using a management methodology based on technological readiness levels (TRL).

*The TRL scale was created in the mid-1970s by NASA (National Aeronautics and Space Administration)[24] in order to identify the readiness level of different technologies in the technological prospecting phase, offering indicators for gauging the evolution of maturity throughout the projects, so as to systematize the management of technological risk and uncertainty. The scale, which is simple to apply, is a 9-level measurement system to assess the maturity level of a particular technology. It includes, from the lowest stage of basic science activities (TRL1) to the highest stage of making the technological solution available to the market (TRL9), indication, according to each level, of which R&D&I activities are required for the evolution of the development process to the next level.*

*Given its success as an indicator for monitoring the execution of projects, the tool was adapted to encompass the particularities of development in sectors other than space, and ended up being incorporated as a metric for the evaluation of public policies to encourage R&D&I by control bodies of the U.S. Congress. More recently, in Brazil, it arrived at the TCU (Tribunal de Contas da União) (Federal Court of Accounts)[25].*

24. This instrument created an objective metric for monitoring space projects, which presented severe difficulties related to the maintenance of public funding sources due to their high degree of uncertainty. National Aeronautics and Space Administration (NASA). "Managing Nasa in the Apollo Era". Available at <go.nasa.gov/3oliSeS>, accessed October 8, 2021.

25. The TCU started to suggest the adoption of the methodology of technological maturity levels to monitor projects of innovative solutions that require the contracting of technological orders. Available at <bit.ly/345GNbr>, accessed on November 18 2021.

| | |
|---|---|
| TRL 1 | Basic principles observed and informed |
| TRL 2 | Applied research: the technology concept and/or its application are formulated |
| TRL 3 | Experimental proof of concept |
| TRL 4 | Laboratory validaed technology |
| TRL 5 | Technology validated in relevant environment |
| TRL 6 | Technology proven in relevant environment |
| TRL 7 | System prototype demonstration in operational environment |
| TRL 8 | Complete and qualified system |
| TRL 9 | Actual system tested in operational environment |

Source: Adapted from "Technological Orders in Brazil: General Guide to Good Practices", available at <bit.ly/3unGuDs>.

Brazil has had industrial and R&D&I policies since 2003[26] that not only places the state in the role of promoting scientific development and R&D&I activities, but that also links the achievement of innovative products or services to the public good and to the progress of science, technology and innovation. Furthermore, those policies provide for the transfer of these benefits to adjacent sectors, and for the generation of training and knowledge for the country.

Next, we will present the constitutional provisions, laws and decrees that shape the legal landscape in this field, and that made it possible, in 2021, to create networks, raise funds and cooperation between players to enable the production of vaccines in Brazil.

# THE BRAZILIAN LEGAL LANDSCAPE

As seen above, the innovative process depends not only on infrastructure (public or private), but also on rules that provide legal certainty and arrangements that mitigate the risk and uncertainty inherent in technological development. The Brazilian legal system allows state intervention on both fronts. In the field of pharmaceutical assistance, Brazil has an industrial policy and a pre-existing infrastructure of public laboratories and science and technology institutes that come together, as presented in the previous topic, to guarantee productive capacity and sufficiency of inputs for the SUS.

In its legislation, Brazil has policies to encourage innovation aimed at reducing risks and uncertainties. The legal framework for innovation was created by Law 10.973/2004, and was reformed by Constitutional Amendment No 85/2015[27]. This amendment changed the wording of Article 219 of the Federal Constitution - which mentioned the internal market as a national heritage - to include the state duty to encourage the formation and strengthening of innovation in companies, public entities, technology parks and centers, and other environments that promote innovation, as well as the creation, absorption, diffusion and transfer of technology.

This amendment also made the duty to promote R&D&I as a concurrent legislative competence of the union, states and

26. For a history of S&T&I policies in Brazil, see: DE NEGRI F. *Políticas Públicas para Ciência e Tecnologia no Brasil: Cenário e Evolução Recente*. Brasília: Ipea, 2021 and GUIMARÃES, R. et. al. "Política de Ciência, Tecnologia e Inovação em Saúde (CT&I/S): uma atualização para debate". Saúde Coletiva 26 (12), Dez/2021.

27. EC 85/2015 represented an innovation by including, among the duties of federated entities, the promotion of means and access to technology, research and innovation (Art. 23,V, CF), elevating them to the category of concurrent competence of all entities. In addition, it expressly expanded the list of competing competences of the Union, states and Federal District to legislate on science, technology, research, development and innovation (Art. 24, IX), granting constitutional authorization for legislative production by the subnational entities. This, in turn, offered regional legislative frameworks to address the peculiarities of the different regions with regard to the promotion and encouragement of R&D&I activities.

municipalities, authorizing the three levels of government to regulate the induction of innovation in a concurrent manner, and allowing greater flexibility in the monitoring and execution of project budgets that had S&T&I activities as their object[28].

Finally, the National Science, Technology and Innovation System was formally established[29]. This system offers means for sharing R&D&I infrastructures and creating synergistic cooperation networks with the aim of mitigating the risk and uncertainty of development in innovation projects.

At the infra-constitutional level, the enactment of Law 13.243/2016 also represented relevant updates in the R&D&I framework, extending the concept of ICT - Instituição de Ciência e Tecnologia (Science and Technology Institution) to encompass private law institutions that meet the legal requirements. It extends to these institutions, such as R&D&I centers of private companies constituted as required by law, special legal systems of tax exemption for the import of machinery and equipment intended for R&D&I activities, or the eligibility of these institutions for funding of public resources for hiring researchers.

This Law also introduced new instruments to foster innovation, such as technological bonuses, financial bonds with or without incentives and the technological order (Art. 19), in addition to facilitating the articulation of strategic partnerships between ICTs and companies. Finally, Decree 9.283/2018 aimed to operationalize and discipline the general regime of instruments provided for in the legal framework for science and technology (Law 10.973/04).

As stated above, the Federal Constitution establishes competing competences for the union, states and municipalities. This implies that these entities can also legislate, in their respective spheres, on the promotion of innovation. In the case of São Paulo, headquarters of the Butantan Institute, Complementary Law No 1.049/2008 establishes the bases for fostering innovation in the state, seeking to encourage institutions (universities, research institutes and knowledge centers), companies, public researchers and inventors to participate in the process of technological innovation. This legal framework provides authorization for the use of existing research institutions, commercialization of patents, licenses, remuneration to inventors, financial support and even state participation in specific purpose companies, investment funds, among others.

Thus, it is possible to conclude that, by promoting the recent revision of the constitutional, legal and infra-legal framework

28. EC 85/2015 offered a mechanism consistent with the specifics of execution of innovation projects, developed from data or incomplete information regarding the development trajectory. Art.167, § 5 of the Constitution is now worded as follows: "The transposition, reallocation, or transfer of resources from one programming category to another may be admitted, within the scope of science, technology, and innovation activities, with the objective of enabling the results of projects restricted to these functions, by means of an act by the Executive Branch, without the need for the prior legislative authorization provided for in item VI of this article."

29. Art. 219-B of the Federal Constitution: "The National System of Science, Technology and Innovation (SNCTI) will be organized in a collaborative regime between entities, both public and private, with a view to promoting scientific and technological development and innovation."

to accommodate the risk and uncertainty of technological development, the Brazilian state offered legal means to manage innovation projects. This provided legal security and incentives to R&D&I in a critical moment of pressure and crisis for the public health system.

# THE TECHNOLOGICAL PROCUREMENT

An important advancement in the Brazilian legal landscape of innovation was the creation of the technological procurement (Encomenda Tecnológica). This toolis a special type of public procurement[30] operated directly by the state and through which, with a single instrument, the state acquires an R&D&I effort aimed at the development of a solution not yet available on the market - or that companies would not make available spontaneously - to meet the public interest.

The law already had other instruments, such as economic subsidy or equity participation, to internalize the risk or uncertainty of development. However, the technological procurement inaugurated a new category of instruments that allow the development of public policies for R&D&I from the identification of the demand[31]. This meant that the entire trajectory of technological development could be included in the contractual object, coupling the development phase with the guarantee of using the state's purchasing power[32] to acquire innovative solutions. There are two very relevant aspects that place this instrument in a privileged position for more radical innovation processes: the identification of a clear public interest need that must be met through the innovative solution, and the diagnosis of technological risk or uncertainty involved in the process.

The technological procurement instrument makes a wide variety of specific procedures that make contracting and monitoring quicker and more flexible, available to the contracting agency and addresses the lack of resources common at the early levels of R&D&I processes, reinforcing the role of taking risks typical of the Entrepreneur State[33].

Finally, technological procurement also reduces transaction costs and barriers to the diffusion of technologies, with a greater degree of novelty, as long as they promote an increase in social

30. IPEA. Nota Técnica N° 71. Diretoria de Estudos e Políticas Setoriais de Inovação e Infraestrutura. Vacina para o novo coronavírus: um caso clássico de encomenda tecnológica. Disponível em <bit.ly/3IZIZ2R>, acesso em 18 de outubro de 2021.

31. A encomenda tecnológica inaugura nova categoria de instrumentos jurídicos de incentivos à C,T&I pois oferece segurança jurídica para organização de políticas públicas baseadas na identificação de demandas da sociedade, posicionando o Brasil em condições semelhantes àquelas praticadas pela União Europeia e EUA para a elaboração e o desenvolvimento de políticas públicas orientadas a missões. A esse respeito, vide: Mazzucato, M. *Mission Economy. A moonshot guide to changing capitalism*. New York: Harper Business, 2021.

32. A realização de compras pelo setor público, dentro de um mix de políticas para a inovação, possibilita a garantia de escala mínima para encorajar os investimentos em P,D&I, sinaliza necessidades não atendidas pelo mercado e pode contribuir para a difusão de padrões e a articulação entre usuários, reduzindo a incerteza de mercado inerentes ao processo de inovação. In: PIMENTEL, V. "Parcerias para o Desenvolvimento Produtivo de medicamentos no Brasil sob a ótica das compras públicas para inovação". Dissertação de mestrado. Rio de Janeiro: UFRJ, 2018, p. 30.

33. MAZZUCATO, M. The entrepreneurial state: debunking public vs. private sector myths. New York: Anthem Press, 2014.

well-being. Two aspects stand out, providing a starker outline of the motivations that led to the technological procurement regarding the Covid-19 vaccines: (i) the identification of technological risk, using the TRL methodology or other assessment tools such as, for example, the clinical trials phases in the case of innovations in medicines, and the accurate technological prospecting carried out by Brazilian public ICTs; and, (ii) the Ministry of Health's commitment to procurement of the vaccine, even while still under development.

As mentioned earlier, Decree 9.283/2018 (in Articles 27 to 30) had the objective of disciplining the general regime for contracting and monitoring the execution of the technological order, thus providing for a much more flexible process than the current one, stated in Law 8.666. It introduced, for example, the waiver of prior public call, allowing the requesting state agency to speed up the contracting process.

Under the technological order, it is possible for the executing institution to negotiate with different suppliers along the trajectory of technology development. That is, depending on the level of knowledge, prior to the execution of the new technology development project, it is possible to contract more than one supplier. This, in turn, paves the way for the development trajectory to be defined based on the new knowledge acquired[33].

Briefly, the technological order is a technology procurement contract in which the state pays for the development of a new product, funds its development and assumes the risk of innovation with the contracted economic agent. The urgent demand for vaccines against Covid-19, caused by the pandemic and the public interest associated with its development, was an important factor in the choice of this instrument. The following section breaks down this process.

34. SALERNO, M.S. *Gestão da Inovação (mais) radical*. 1a ed., Rio de Janeiro: Elsevier, 2018.

# AS VACINAS CONTRA A COVID-19: O CASO BRASILEIRO

After the analysis of the legal scenarios that made the procurement, public production and distribution of vaccines in Brazil possible, as well as the scenario that laid the foundations for instruments such as the procurement of technology to be applied to the Brazilian case, it is now necessary to clarify how these factors were applied, by health managers at the federal and state levels, to execute the two technology transfer contracts in Brazil between 2020 and 2021.

The history of the fight against Covid-19 in Brazil can be summarized, on the one hand, by the lack of strong and centralized measures by the federal government to reduce infection (encouraging the use of masks and promoting physical distancing, for example) and of the acquisition of vaccines in adequate volume and time; and, on the other hand, by activating existing physical, institutional and regulatory structures to boost local vaccine production.

Regarding the first point, there is widespread internal and external criticism of the handling of the crisis[35], evidenced by the Brazilian government's delay in acting to protect lives, promotion of ineffective or unproven treatments against Covid-19, and the Federal Supreme Court's (STF) decision to demand the federal government to present an action plan.

35. VENTURA, D; AITH, F; REIS, R. "Crimes against humanity in Brazil's Covid-19 Response: A Lesson To Us All", BMJ, 2021; 375:n2625 doi:10.1136/bmj.n2625

Despite the lack of action by the Executive power, attention is drawn to the fact that, in November 2021, more than 314 million doses of vaccine had been administered. This represents 136 million people, or 64% of the Brazilian population, with two doses. This achievement is directly related to the second point: the responsiveness of the national structure for local vaccine development and production. This topic focuses on two protagonists in this process, Fiocruz and Instituto Butantan.

Still in the first half of 2020, these institutions identified the degrees of technological maturity reached so far by the most promising vaccines, and established technology transfer contracts with the aim of contributing to the final stages of their development. They aimed not only to offer them to SUS, but also to incorporate new technologies to enable local production.

It is important to mention that, from the perspective of R&D&I activities that demanded greater investments, especially those of a public nature (direct or indirect), there was a predominance of countries traditionally known as holders of the largest number of patents in the pharmaceutical industry. Brazil, although not one of these countries, is listed as one of the first countries to have procured vaccines[36], especially from AstraZeneca.

36. In the data consolidated by the Knowledge Portalia platform, there is an indication of a single vaccine procurement contract, in the estimated value of U$S 943 million, whose contract was announced in June 2020, prior to the announcements of vaccine acquisition by the US government (whose first acquisitions are reported in August and September 2020). Available in <bit.ly/3AVu0E8>, accessed November 20, 2021.

The Fiocruz technology procurement agreement was celebrated under the technological procurement format, as described in a previous topic, with the provision of supplying a first batch of 100.4 million doses, produced locally and destined for the PNI in the first semester of 2021.

Already considering the internationalization of technology through technology transfer for the production of national API (Active Pharmaceutical Ingredient), the order predicted that another 110 million doses of vaccine would be made available to SUS in the second half of 2021.

The price per dose agreed in the negotiations of the technological order was US$ 3.16 for the Oxford/AstraZeneca vaccine. As a comparison, in neighboring countries)[37] such as Colombia and others in Latin America, which had not negotiated technology transfer terms yet in 2020 and had focused on contracts for the procurement of ready-made vaccines, negotiations were only concluded in the second half of 2020, with prices varying from US$4 to US$6 per dose. Even in countries with large purchasing capacity, including the US, the AstraZeneca vaccine was traded at $4 per dose at a time subsequent to the Fiocruz contracting.

The extraordinary budget resources necessary for the conclusion of the agreement were guaranteed through two legal instruments: MP 994/2020 and Law 14.107/2020. With these authorizations, R$ 1,994,005.00 was allocated to the celebration of the technological order contract[38] between Fiocruz, Bio-Manguinhos and the pharmaceutical company AstraZeneca UK Limited, given the recognition[39] by the Ministry of Health of Fiocruz as an entity qualified to promote the absorption of technology and the local production of the vaccine developed by the University of Oxford.

Publication of the results of AstraZeneca's first and second clinical trials involving their Covid-19 vaccine, which attested to its ability to produce a reaction in the immune system, satisfied the technical conditions and legal and juridical requirements. So, the technological ordering contract was signed in record time. The object of the contract was the access to doses and the production of the finished vaccine using imported raw materials, in addition to the commitment to carry out technological transfer for the production of the vaccine in Brazil from a national API.

Specifically, the technology order contract was drawn up in the form of a term that has general obligations between the parties and three annexes[40]. It provided for specific obligations which deal with the technical aspects of the execution of the project, whose contents, for reasons of secrecy and security, are not public.

37. Unicef gathered data through the Covid-19 Vaccine Market Dashboard, which tracked prices around the world through supply contracts for the main vaccines already approved. For the Brazilian case, it is possible to verify that, in relation to other vaccines authorized by Anvisa, the price of the Oxford/AstraZeneca vaccine developed together with Fiocruz represents a lower unit price compared to Pfizer/Biontech (U$ 10) and Sinovac/ Coronvac ($10.30). Available at <***uni.cf/3glnjlC***>, accessed November 20, 2021.

38. Technological Procurement Contract nº 01/2020 - Technological Procurement Agreement entered into by the Oswaldo Cruz Foundation (Fiocruz), the Institute of Technology in Immunobiologicals (Bio-Manguinhos) and AstraZeneca UK Limited.. Available at <***bit.ly/3ro9R6T***>, accessed on October 10, 2021.

39. Considering the technical criteria for contracting a technological order, the designation made by the Ministry of Health, through official letter Nº 743/2020/DATDOF/CGGM/GM/MS of 06/26/2020, recognized Fiocruz with noteworthy technological and industrial competence in the production of vaccines for the absorption of technology, and local production of the vaccine developed by the University of Oxford against the coronavirus (ChAdOx nCov-19). Based on this recognition, the subsequent steps for contracting a technological order could be shortened, under the terms of Decree 9,283/2018, in order to face the sense of urgency imposed by the effects of the Covid-19 pandemic.

40. The annexes, which form an inseparable part of the contract, are as follows: Annex I - Research, Development and Innovation Project for the stages of industrial scale-up and final processing in Brazil of the Covid-19 Vaccine ("PD&I Project"); Annex II - Terms and Conditions for the Production and Delivery of the Active Pharmaceutical Ingredient (API); Annex III - Technology Supply.

In terms of general obligations, AstraZeneca was responsible for the total transfer of technology to Fiocruz, in an initial period of up to one year, so that Fiocruz could develop the scale-up of the technology transferred for local production of vaccines from the supply of API by AstraZeneca. In a second phase, with the conclusion of the technology transfer, vaccines would be produced locally with API produced by Fiocruz in Brazil. At the other end, Fiocruz and its executing arm (Bio-Manguinhos) were assigned the duties of preserving technological confidentiality, transparency as to the results obtained locally, the establishment and observation of a governance policy to monitor the project, and reporting partial results. In addition, they had the specific obligation to ensure that the vaccine produced locally was not sold, distributed, supplied or marketed outside the territory served by SUS, as a way to safeguard the Brazilian territory, at least during the pandemic period.

In the case of the Butantan Institute, the technology transfer contract signed with the Chinese pharmaceutical company Sinovac was not publicly available. However, its signature was reported on 9/30/2020, and the document provided for the initial supply of 43 million doses of the Coronavac vaccine.

According to the Institute's[41] official sources, with the Covid-19 pandemic, its technological prospecting sector sought an international partnership to develop a vaccine against the new coronavirus that included the internationalization of technology. That is, they sought a partnership that allowed the Brazilian laboratory to participate in the development process. This led to the partnership with the Chinese company Sinovac, which included conducting phase 3 clinical trials in Brazil, registration of the vaccine at Anvisa by Butantan, and the start of production in December 2020.

41. Available at <bit.ly/34dHcsi>, Accessed on November 8, 2021

The initiative included investment in a new industrial plant for the production of vaccines with biosafety level 3, guaranteeing the Institute the possibility of producing Coronavac from its initial stages. The new manufacturing unit is officially scheduled for completion in 2022.

The agreement between Instituto Butantan and Sinovac was a technology co-development contract and involved the legal support of the Institute's support foundation. Within the challenging scenario of growing numbers of cases and deaths resulting from Covid-19, the technology prospecting sector worked to find a product that was already in an advanced stage of development and that, at the same time, involved technology transfer to domestic production. Thus, the inactivated virus vaccine, which at the time was undergoing a phase 3 clinical trial, was chosen.

The Institute, therefore, also coordinated all the tests in Brazil. As in the case of the Oxford vaccine with Fiocruz, this stage of development had the collaboration of other ICTs, especially public universities and public hospitals of reference in infectology, such as Hospital Emílio Ribas in São Paulo.

The choice proved to be the right one and culminated in the registration of Coronavac, which was fundamental to the Brazilian immunization strategy against Covid-19. Subsequently, Butantan started a new project, still under development, for the Butanvac vaccine, which would include the entire clinical stage of development. Challenges and uncertainties associated with phase 1 and 2 clinical trials have not yet allowed the project to move forward. This reiterates the relevance of the option for Coronavac, which was already at an advanced level of development.

In the case of Fiocruz, on the other hand, it is worth presenting the arrangements as cooperation networks. Sometimes, these arrangements are among international partners and organized as innovation ecosystems under the general leadership of a company that acts as the project leader. Such arrangements may be structured as development platforms, as seen in the experience with Oxford University[42], In cooperation with the pharmaceutical company AstraZeneca, with direct public funding from the United Kingdom and indirect funding from Cepi (Coalition for Epidemic Preparedness Innovations), this project promoted the maturation of the biotechnological platform already existing at the university to develop a specific application against the Sars-CoV-2 virus.

Especially in more radical innovation initiatives, the adoption of the model of technological development platforms[43] has characteristics of more flexible organizations which go beyond the formal boundaries of an institution or supply chain. Unlike traditional arrangements for the development of updated versions of the same product, the perspective of creating a groundbreaking immunization product demands the organization of strategic partnerships that are oriented in the form[44] of an innovation ecosystem. In this model, the interfaces between their members are predominantly open, with the sharing of competences and R&D&I infrastructures, in which the control and management systems are backed by governance rules in order to accommodate risk and uncertainty.

Thus, considering the peculiarities that the dynamics of developing a new vaccine require, and the urgency of a health response, the preference for adopting governance mechanisms over specific contractual[45] rules, functional hierarchy, open

42. Available at <bit.ly/3unDZRK>, accessed 20 November 2021.

43. Technological platforms can be understood as cooperation networks between technology suppliers and developers that are structured under the leadership of a company that coordinates efforts, generates cooperation between the various stakeholders and provides conditions for the co-creation of value. For the development of more radical innovations, according to SALERNO (2018), GAWER (2014) and CONNOR (2018), project management models structured in the form of technological platforms have shown greater chances of success. Specifically, for the case of developing a vaccine against Covid-19, the pre-existence of Fiocruz's network of technological platforms as a strategic axis of the institution is significant. Available at <bit.ly/3ofW5kH>, accessed on January 12, 2022.

44. GAWER "Bridging Differing Perspectives on Technological Platforms: Toward an Integrative Framework". Research Policy, 43 (7), pp. 1239 -1249. Available at <bit.ly/3sjnCTE>, accessed September 8, 2021.

45. GILSON, R.J. SABEL, C. F., SCOTT, Robert E. "Contract, Uncertainty and Innovation". Columbia University Law School – Law & Economics Research Paper Series No. 385 and Stanford University Law School – Law & Economics Research Paper Series. Paper No. 403. Available at <bit.ly/3J2G35p>, accessed September 8, 2021.

interfaces between partners, and consensus as a guideline to mitigate conflicts, took on particular relevance. These cooperative arrangements and governance models with open interfaces have undoubtedly contributed to the speed of vaccine scale production[46] The terms referring to the negotiation of intellectual property rights were dealt with in a specific instrument, through a technology transfer agreement registered[47] with Inpi, *Instituto Nacional da Propriedade Industrial* (National Institute of Industrial Property).

Possible delays in the production of a national API can be understood as associated with development risk and the complex chain of suppliers and international certifications that must be met for the approval of the raw material. Thus, it is possible to observe that the procurement of vaccines in development converged with the R&D&I efforts undertaken in the nationalization of the technology, without damaging either the positive externalities for Brazil for the generation of local capacity, or the possibility of building up local supply chains.

The positive results of these contractual designs contrast radically with the lack of coordination at the federal level to face the pandemic, and were only made possible by the combination of public policies, infrastructure and pre-existing expertise in public laboratories, in addition to the use of purchasing power and PNI and science, technology and innovation strategies. These factors may have represented advantages over other countries that did not have legal instruments or R&D&I capacity installed to face the crisis created by the pandemic in the first months of 2020.

46. According to data from Fiocruz, less than three months had elapsed since the confirmation of the partnership between AstraZeneca and the University of Oxford for the scale production of the vaccine. Available at <***bit.ly/3onWPnN***>

47. In a phase, subsequent to the development of the object of the technological order, there is an associated technology transfer contract between Fiocruz and the pharmaceutical company AstraZeneca UK Limited, whose object is the technological supply of the final processing necessary for scaling up the production of the active pharmaceutical ingredient (API) for the production of doses in the quantity necessary for access to the population in a pandemic period, with a presented value of US$ 25 million. Application number: BR 70 2020 000402-9, with protocol number 8802000001930. Consultation carried out with the Inpi database, available at <***bit.ly/3ASpDKj***>, accessed October 20, 2021.


# FINAL REMARKS

Brazil was severely affected by the Covid-19 pandemic, losing more than 600,000 lives and standing out as an example of mishandling, especially by the federal administration. Even so, the country managed to sign two relevant technology transfer agreements for the public production of vaccines (Coronavac/ Sinovac and Oxford/AstraZeneca) and, despite the delays in starting the immunization program, managed to execute it relatively quickly.

Brazil's relative success is based on institutional and economic structures consolidated in the country over the last decades and is associated with its Unified Health System (SUS), especially the National Immunization Program. This program includes the centralized procurement of immunizers by the Ministry of Health, the public pharmaceutical laboratories, and the legal landscape that allowed the contracts to be signed.

All these instruments may be taken into consideration within a broad idea of the right to health, as they allow the state to act to ensure access to the vaccine from a very early stage, which includes research and the development of immunizers.

The PNI, which has existed for more than four decades, is featured by the Ministry of Health and distributed across the territory using primary healthcare infrastructure.

A significant part of the PNI is supplied by public laboratories, especially Bio-manguinhos/Fiocruz and Instituto Butantan. The influx of funds from centralized purchasing, among other factors, historically provided these institutions with the economic stability to produce and carry out technology prospecting activities, resulting in a successful institutional arrangement that not only ensures health technologies at reduced prices to the Ministry, but also boosts national technological development and capacity.

Specifically in the context of Covid-19, Fiocruz entered into a partnership with the pharmaceutical company AstraZeneca for technology transfer, including API manufacturing. This was a unique example of arrangement, which shows that alignment between institutional mission and pharmaceutical innovation can be useful to mitigate conflicts of interest and establish functional governance structures for innovation, including radical innovation.

The Butantan Institute, on the other hand, signed a partnership with the company Sinovac, which also included technology transfer. The contracts were only possible due to the legal structure existing in the country, especially the provisions that

allow the procurement of technology, i.e., contractual forms in which the state funds the development of a certain technology, assuming inherent risks of the process.

The Brazilian case must also be analyzed critically based on its limitations, which are related to the predisposition of private companies to transfer technology voluntarily. All the legal and economic instruments used by the state, in the development and production of vaccines against Covid-19 in the cases analyzed, were based on voluntary technology transfer agreements, which have limitations. It is also possible to explore different paths that give room to local production, such as the suspension of intellectual property rights, especially patents and industrial secrecy.

Going through the long path of Brazilian legal evolution in recent years, it is possible to identify the expansion of the list of legal instruments that allow the internalization of the risk and uncertainty of technological development, especially in cases of more radical innovations. Harmonized with the purchasing power of the Brazilian State, these instruments pave the way for promoting access to disruptive innovations for the whole of society and give Brazil significant advantages in relation to other countries that do not have legal instruments or installed production capacity to face the pandemic. Finally, they highlight the importance of the Brazilian State continuing to focus on the innovation and production of vaccines and medicines of interest to the population.

Idec understands that supporting the right to health also requires investment in public policies of technological innovation and industrial training, and that the public production of vaccines is a fundamental element of the success of immunization strategies in Brazil, as can be seen in the case of the Covid-19 pandemic. The Brazilian case illustrates how the state has a leading role in pharmaceutical innovation and that its power must be directed to the public interest.

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