The Economic-Industrial Health Complex and Local Drug production: a case study of organizational sustainability

Complexo Econômico-Industrial da Saúde e a produção local de medicamentos: estudo de caso sobre sustentabilidade organizacional

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ABSTRACT The article analyzes the Brazilian industrial policy for the health sector in the last two decades by describing the conditions of organizational sustainability vis-à-vis the induction of the Ministry of Health's Partnerships for Productive Development (PDP). The case study of a large Official Pharmaceutical Laboratory (LFO) identified unanticipated effects caused by governmental induction in the industrial area. The use of the case study method was essential for the analysis of organizational issues that cannot be accurately explained by simple quantitative description. It is shown in the article that PPDs have successfully expanded the productive capacity of the public sector in the pharmaceutical area. However, PPDs results should be carefully evaluated in the case of Farmanguinhos. The article concludes that the production unit of Fiocruz (Oswaldo Cruz Foundation) will probably face serious challenges regarding sustainability. Government purchases under PPDs did not favor gains in scale or scope, negatively affecting the LFOs with high production capacity, as is the case of Farmanguinhos.

KEYWORDS Public policy. Drug industry. Laboratories.

RESUMO *O artigo objetivou a análise da política industrial brasileira para o setor saúde nas últimas duas décadas por meio da descrição da condição de sustentabilidade organizacional vis-à-vis à indução da Parceria para o Desenvolvimento Produtivo (PDP) do Ministério da Saúde. O estudo do caso de um grande Laboratório Farmacêutico Oficial (LFO) identificou os efeitos não antecipados associados à indução governamental na área industrial. O estudo de caso foi a opção metodológica para a análise de questões de natureza organizacional que não podem ser explicadas com precisão pela descrição quantitativa. Como resultado, o artigo aponta que a PDP foi bem-sucedida na ampliação da capacidade produtiva no setor público na área farmacêutica. Contudo, para o caso de Farmanguinhos, os resultados da PDP devem ser avaliados com cautela. O artigo conclui que a unidade produtiva da Fundação Oswaldo Cruz (Fiocruz) enfrentará sérios desafios à sustentabilidade em função da sua singular inserção na PDP. As compras governamentais promovidas pela PDP não favoreceram ganhos de escala e escopo, afetando negativamente os LFO com elevada capacidade de produção, como é a condição de Farmanguinhos.*

PALAVRAS-CHAVE *Política pública. Indústria farmacêutica. Laboratórios.*

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Introduction

This article aims to analyze the impacts of the Brazilian Ministry of Health's Partnerships for Productive Development in Health (PDP, acronym in Portuguese) on the sustainability of the Pharmaceutical Technological Institute (Farmanguinhos), the federal pharmaceutical laboratory hosted by the Oswaldo Cruz Foundation (Fiocruz). The relevance of studying the specific case of Farmanguinhos is due to its pioneering actions in the local production of antiretrovirals for the Brazilian Aids program, launching a successful trajectory for the incorporation of technology by the Brazilian Public Health System (SUS)[1].

With the case study of Farmanguinhos, attention is called to the threat to the sustainability of large Official Pharmaceutical Laboratories (LFO, acronym in Portuguese for Laboratórios Farmacêuticos Oficiais) caused by the high spread of medicine acquisition under PDPs. Due to the important connection of PDP modelling with the Ministry of Health high-cost medicine purchase policy[2], government interests in the decision-making process are also important, promoting a fragmentation of the public market of medical supplies.

The PDP model is a Brazilian Federal government policy initiated in 2008, which seeks to develop new technological skills for LFOs[3]. By the beginning of 2019, the Ministry of Health had held five competition rounds for the selection of PDP projects, during the administrations of then presidents Lula (2009 and 2010), Dilma Rousseff (2011, 2013, and 2015) and Michel Temer (2017)[4].

A PDP is established between two or more public institutions and private companies, for the development, transfer, and incorporation of technology, and the production of materials and strategic medicine to meet the demands of SUS[3]. It enabled public laboratories to intermediate the purchases of medicine or other products by the Ministry of Health from private companies through a Decentralized Implementation Term (Termo de Execução Descentralizada – TED), or through an agreement (in the case of state government laboratories)[4].

It is important to highlight that in the PDP model, the scope and the production scale of LFOs – such as Farmanguinhos – depend on the decisions made by the Federal government. With centralized purchases, the Ministry of Health also has the prerogative of being the single purchaser (monopsony), defining the conditions of production and the portfolio of public and private producers[3].

The provision of incentives to improve Brazilian technological skills intends to respond to the structural deficit in the commercial balance produced by the imports of medicines and other medical supplies[4]. In this context, the PDP policy has focused on creating conditions for local production in order to ensure access medication, as well as strengthening the so-called Brazilian Industrial and Economic Health Complex. PDPs thus answer the demands for technological expansion of the health sector and the encouragement of inclusive and competitive development, which also favors the positioning of the country in the global scenario[5].

The PDP policy also concerns the exponential growth of expenditure on new medicine and products for the SUS, which limits the coverage of strategic programs, such as the free distribution of antiretrovirals[6].

Especially due to the constitutional right to health in Brazil, PDPs aim to reduce expenditure on the acquisition of medicine and products for the SUS. The idea of social citizenship encompassed in the Brazilian Constitution has produced positive effects in terms of access to benefits and services in education, assistance, health, and social security.

In this context, this constitutional right to health has imposed the Executive

Government to commit to quickly respond to judicial demands for high cost medicines and materials. In addition to the pressure of the community of health specialists, as noted by Lago and Costa[7], and the political mobilization of the society emphasized by Parker[8], the Brazilian public health sector has responded to demands for high cost technological incorporation in individual health care due to legal impositions[9].

PDPs therefore seek to mitigate the vulnerability of the Ministry of Health in the acquisition of strategical raw materials and reducing the Brazilian technological and productive dependence *vis-à-vis* legal demands for health care in an accelerated technological environment. The dynamics of innovation in terms of health products and medicine can have a short technological lifecycle, resulting in precocious obsolescence and disposal. This aspect is directly associated with the evolution and absorption of technological advances[9].

Finally, it is worth considering the pressure exercised by intellectual property rules on local policies aimed at guaranteeing access to innovative and high cost medicines, such as the most recent generation of antiretrovirals. Not rarely, the formalization of universal access to pharmacological treatment in Brazil has resulted in clashes with supranational intellectual property rules and the patent rights involved in high cost medicines[10].

What calls attention in the PDP policy is that it emerged in a context posterior to the Trips Agreement (Agreement on Trade-Related Aspects of Intellectual Property Rights) and the new intellectual property regulation[11], encouraging the formation of coalitions for technological transfers between private multinational companies and LFOs previously limited to the vaccine sector[12].

Material and methods

Case studies allow the description of singular questions of organizational dynamics, which cannot be explained with any reasonable degree of precision by the analysis of institutional or systemic context, or quantitative indicators. The Farmanguinhos case study describes the constraints on the ability of a government laboratory to adapt to the technological internalization policy. The present case study takes references the technically specific productive functions of Farmanguinhos in the PDP model, based on previous studies which described the unit's position in the local production of strategic medicines.

Three procedures were adopted for the gathering of primary data: a) document review regarding the implementation of the PDP policy and contextualization based on the literature; b) analysis of revenue indicators, the production of pharmacological units, and the portfolio of medicines offered by Farmanguinhos and c) the description of Farmanguinhos' demands in the PDP proposal selection rounds.

In this article we assume that the PDP policy changes profoundly the position of LFOs in governmental purchases. To measure the effects of these changes, we adopt the Hirschman-Herfindahl Index (HHI), which allows the identification of the dispersal/concentration pattern of PDP projects after the evaluation rounds. The HHI measures the concentration – or lack of it – of a market or sector of the economy. It is obtained by squaring of the proportional (%) sum of the participation of each company in a distribution of sectorial activity or the production of products with similar characteristics.

For the analysis of the variation of the annual quantity of pharmaceutical units produced by Farmanguinhos, the article uses the log-lin model described by the equation ln Yt = β1 + β2t + ×t. This model is like any other linear regression in which the parameters β1 and β2 are linear. In this case the difference is that the regression is the logarithm of Y and the independent variable is time, represented by 't', which will assume the values 1,2,3, +...+ n, [...], corresponding to the period analyzed[13].

Results and discussion

The institutional context of PDP

PDP's wide-ranging development and technological innovation agenda has benefitted from initiatives of industrial policy in the last two decades, in a democratic context: i) the 2003 Industrial, Technology, and Foreign Trade Policy (PITCE), which defined the pharmaceutical productive chain as strategic since it brings together crucial technologies, such as nanotechnology, biotechnology, and fine chemistry; ii) the Productive Development Policy which selected the health complex as one of the six strategic areas iii) the 'Greater Brazil' Plan which choose the health sector as a strategic segment for the country and established the directives for implementation of partnerships for productive development and the use of the purchasing power of the state as an induction instrument[14].

Gadelha and Costa[5] also highlights the Action Plan for Science, Technology, and Innovation 2007-2010 from the Ministry of Science and Technology which selected the health sector as strategic under the National System of Science, Technology, and Innovation. The actions of the Department of the Industrial and Innovation in Health Complex (Deciis) from the Secretary of Science, Technology, Strategic Raw Material of the Ministry of Health, created in 2009, were also essential in allocative decisions aimed at development and innovation.

With the Deciis, the Ministry of Health is entitled to create agreements regarding technological transfers from Private Brazilian and multinational companies to LFOs[14]. As a result of this, PDPs were able to follow an independent agenda from the BNDES (the Brazilian National Development Bank) through the Support Program for the Development of the Pharmaceutical Productive Chain (Profarma)[15].

Two legal innovations under the auspices of public administrative law allowed, in the institutional sphere, the intervention of Deciis in the public offer of strategic medicine: i) the Public-Private Partnership Law (Law no. 11.079, dated 30 December 2004), which instituted the so-called sponsored and administrative concessions, bringing new possibilities and limits to the exploitation of governmental ventures by third parties and ii) the Innovation Law (Law no. 10.973, dated 2 December 2004), which allowed the creation with private companies of various types of strategic partnerships of public agencies for the development of industry and the increase of the Brazilian technological autonomy[16].

This arrangement indicates the complexity of the development of sectorial industrial policy, based on LFOs and private Brazilian and multinational companies in the dispute for the Ministry of Health's purchases of medicines and products. The PDP model has been seen as a successful example of the combination of industrial and social policy to ensure the local production and provision of strategic medicine for the public sector[17]. Previous studies showed that the only recognized successful experience of industrial policy was during the Brazilian dictatorship period (1964-1985)[18].

Nevertheless, it should also be highlighted that the concern with the collateral effects of the actions of the federal government on private organizations and governmental productive units was not considered when the agenda was prepared, or in the rare attempts to evaluate PDPs. This finding is unsurprising due to the presence of clearly nonproductive PDP mechanisms for scale (productive efficiency) and scope (diversity of products).

Curiously, the formation of the PDP agenda does not mention any strategic public laboratories and companies for the local production of health products. Only the taxation, regulatory, and tendering dimensions are identified as significant barriers to the development of Ceis[9].

Similarly, Gadelha and Temporão[19] assess PDP from a systemic perspective, leaving aside

any reflections on the responsive conditions and sustainability of LFOs and private companies given the adaptative pressure proposed by the Ministry of Health's innovation agenda. In the organizational analysis perspective adopted in this article, the understanding of the decision making context and of the adaptive capacity of LFOs is essential to the policy of isomorphic induction. Powell and Di Maggio's[20] theory of isomorphism emphasizes the understanding of the official process which obliges a given element of a population (of individuals or organization) to resemble another in answer to the demands of the institutional environment.

The question which guides this article is that the Ministry of Health, by adopting a distributive approach to assess the PDP model, ignoring the asymmetry of productive or organizational unused capacity, could have caused LFOs to become unsustainable due to the loss of scale. However, we understand that the spread in the PDP decision making process was undoubtedly the result of institutional constraints associated with a federative pact.

Samuels[21] highlights the importance of the Brazilian federalism in understanding the decision making processes. According to him, federalism configures regional political ambitions and the effects of this ambition leads the country's broader decision making process. As a result, the constraints and incentives for political survival at the regional level interfere in national initiatives. Thus, it is important to highlight that, even though the Ministry of Health is the exclusive purchaser, the PDP decision making process does not occur in an institutional vacuum. On the contrary, public companies legitimately influence the decisions of public agents.

It is acknowledged that the definition of budget sources and private competencies for the health sector by regional and local governments is also part of the strategy of constructing the influence of federal interest groups over national decisions. Constitutional connections have expanded the participation of regional and local governments in the funding of health policy and the allocation of the resources necessary for programs nationally defined as priorities in the last two decades[22]. Financial commitments of states and municipalities resulted, as foreseen, in the increased influence of the federal government on the formation of the national health agenda, as in the case of the local production of medicines. It is worth noting that the centralization of the acquisition and distribution of high cost medicines in the SUS, occurred in 2007, was a decision agreed between the Ministry of Health and state governments[2], making centralized purchases by the federal government possible since 2008 under PDPs.

The presence of public laboratories in the production of antiretrovirals in the middle of the 2000s indicated the growth of the interest of regional governments in the local production of high cost medicine. As shown by Lago and Costa[23], the public laboratories Lafepe (Pernambuco), Iquego (Goiás), Furp (São Paulo), Funed (Minas Gerais), and Lifal (Alagoas) received significant share of the local production of antiretrovirals in the current decade. The new entrants to the relevant public market for the supply of antiretrovirals led to the decline of the leading position of Farmanguinhos as a supplier for the Ministry of Health.

Farmanguinhos and PDP

The technological ascension of Farmanguinhos for the development of the pharmaceutical industry occurred within institutional possibilities and limits by late 1990s. Between 1998 and 2000, Farmanguinhos reverse engineered the six medicines of AIDS treatment cocktail – Didanosine (pill), Stavudine (capsule), Lamivudine (pill), Zidovudine (capsule), Nevirapine (pill), and Indinavir (capsule) –, becoming capable of identifying and producing their raw materials. In addition to antiretrovirals, Farmanguinhos produced

1375 billion pharmaceutical units in 2002 – medicine for continuous use of diseases of the cardiovascular and central nervous systems and for the hypertension and diabetes programs[1].

The non-existence of protection for intellectual property (only formalized by Intellectual Property Law no. 9.279, from 1996) allowed Farmanguinhos to advance some research and development stages in the production of antiretrovirals. The literature identifies four Research and Development (R&D) stages for medicine: the first, with higher technological demands, is the research and development of new active principals (drugs); the second is the industrial production of drugs; the third stage is the production of medicine; the fourth is publicizing and commercialization[24].

Pinheiro[24] highlights that at that time Brazil only had the third and fourth stages due to the delayed development of R&D related to medicine. By late 1990s, the author showed that the lack of investment in the first and second stages by companies, and the international recognition of patent laws, placed developing countries, including Brazil, in a situation of critical dependence on exogenous technological transfer[24]. In less than a decade, the technological leadership of Farmanguinhos was challenged by the entrance of new drugs for Aids treatment, protected by the new patent regime and imported medicine[23].

PDPs created an unprecedented institutional scenario for government producers by establishing horizontal cooperation with the leading innovative companies in this sector, including multinationals. However, Farmanguinhos joined the PDPs barely controlling the two fundamental pillars of sectorial innovation, as suggested by Malerba[25]: institutional conditions (the interests of state governments prevailed in PDP decisions) and the technological scenario (the unit had already lost its technological leadership position in the production of antiretrovirals).

In these conditions, to the contrary of what Gadelha and Temporão[19] suggest, Farmanguinhos was not especially favored by the PDP policy. The examination of project selection rounds reveals that the preferences of the federation prevailed *(table 1)*. In the seven PDP Calls for Tenders, 76% of the approved projects were in public laboratories.

Table 1. Share of State Laboratories in PDP projects approved by MS – 2009-2017

Year of Call for Tenders	Total of public agencies participating in approved projects	Total of State Labs participating in approved projects	% share of State Labs participating in approved projects
2009	11	7	64
2010	8	5	63
2011	10	6	60
2012	32	24	75
2013	37	32	86
2015	12	6	50
2017	37	32	86
Total	147	112	76

Source: Ministry of Health [http://portalms.saude.gov.br/ciencia-e-tecnologia-e-complexo-industrial/complexo-industrial/parceria-para-o-desenvolvimento-produtivo-pdp]. Accessed on 27/12/2018[26].

Table 2 shows that Farmanguinhos was especially successful in the various PDP competition rounds because an average 76% of submitted projects were approved between 2009 and 2017. Other LFOs had average 45% of projects approved.

Some of Farmanguinhos' approved projects had a high convergence with the unit's technological trajectory, especially in the production of antiretrovirals. However, contrary to Biomanguinhos for example, none of Farmanguinhos' projects aimed to developing new technological routes for biological medicines with distinct knowledge bases from the ones used in the majority of LFOs.

Of importance here is the observation of Torres, Hasenclever, and Nascimento[27] that in this context the biotechnological route demands knowledge of molecular biology, genetic engineering, and cell cultivation, reinforcing the need for connections with basic science in the trajectory of sectorial innovation.

Table 2. Distribution of projects submitted and approved from public laboratories and Farmanguinhos under PDP, 2009-2017

Year of Call for Tenders	Total projects submitted by public laboratories (a)	Total projects from public laboratories approved (b)	% of approved projects (b/a*100)	Total projects submitted by Farmanguinhos (c)	Total projects from Farmanguinhos approved (d)	% projects from Farmanguinhos approved / total projects submitted by Farmanguinhos (d/c*100)
2009	25	11	44%	8	3	38%
2010	66	11	17%	2	1	50%
2011	25	10	40%	3	3	100%
2012	46	25	54%	6	6	100%
2013	137	99	72%	7	3	43%
2015	34	8	24%	1	1	100%
2017	80	37	45%	4	4	100%
Average 2009-2017	59	29	42%	4,5	3	76%

Source: Ministry of Health[28].

It can be seen in *table 2* that in the 2009-2017 Calls for Tenders, Farmanguinhos participated in 7.5% of the total of 413 projects submitted by LFOs. As the competition is selective, surprisingly residual in comparison with the global offer of competing public laboratories, for four years in a row Farmanguinhos had an elevated project success rate, although the loss of leadership under PDPs seems evident.

It is also worth calling attention in *table 2* that in the 2015 Call for Tenders, the number of projects approved by PDPs for all LFOs was less than two digits. In this round, the changes introduced in the project evaluation mechanism by Edict no. 2531, dated 12 November 2014, expanding PDP governance, had a decisive influence on the 2015 result. Farmanguinhos obtained approval for one project. Furthermore, the amount of projects presented by the unit was residual in relation to the total set of competing public agencies, which submitted 34 proposals in 2015.

In 2017, the new post-impeachment coalition in the Federal Executive did not lead to the dismantling of PDP and maintained the

position of public laboratories. In the 2017 Call for Tender, Farmanguinhos had four projects approved (100% of those submitted). In the 2017 round, public laboratories submitted 80 projects, with an approval rate of 45%.

The competitive presence of public laboratories conformed to a pulverized model of competition for federal government purchases under the auspices of PDP. As *table 3* shows in 2017, for example, the value of the HHI of 957 for the distribution of future purchases of medicine by MS proved the notable dispersal of the distribution of ownership in the supply of strategic medicines. An HHI lower than 1500 indicates the shaping of a pattern of supply with many companies, as shown in *table 4*. An HHI between 1500 and 2500 indicates a moderate concentration, while a score of above 2500 indicates concentration.

Table 3. Distribution of governmental acquisitions by public laboratories under PDP in the 2017 round

Public Laboratory	Frequency of Projects Approved	%
FARMANGUINHOS	5	14
LAFEPE	5	14
IVB	4	11
LQFA	4	11
NUPLAM	4	11
BIOMANGUINHOS	3	8
TECPAR	3	8
BUTANTAN	2	5
FUNED	2	5
LFM	2	5
BAHIAFARMA	1	3
FURP	1	3
LQFEX	1	3
TOTAL	37	100
HH index	957	-

Source: Ministry of Health[29].

In this scenario, the adaptive effort by PDP brought timely results to Farmanguinhos by allowing the growth of the average value of pharmaceutical units produced, as *table 4* shows. This growth in the aggregate value of the mix of products indicates an important change in relation to the prices practiced by Farmanguinhos in the previous decade, when the values of pharmaceutical units were priced in cents of the US dollar[1].

It is also worth highlighting in *table 3* that public laboratories which migrated to the biological medicine platform (such as Bio-Manguinhos and Tecpar) had revenue from the production of medicine 52.5 times higher than the maximum obtained by Farmanguinhos.

Table 4. Products from Farmanguinhos, Tecpar, and Biomanguinhos acquired under PDP – 2014/2018

Product	Laboratory	Therapeutic Class	Plataform	Acquisition Date	Value in US$ on date of acquisition
Atazanavir (Cápsula 200 mg)	Farmanguinhos	antiretroviral	antiretroviral	25/07/2014	1,60
Atazanavir (Cápsula 300 mg)	Farmanguinhos	antiretroviral	antiretroviral	25/07/2014	2,97
Cabergoline	Farmanguinhos	prolactin inhibitor	synthetic	07/04/2016	2,50
Pramipexol	Farmanguinhos	Anti-Parkinson's	synthetic	10/10/2014	0,13
Rifampcim + Isoniazid + Pirazinamide + Etambutol (4 em 1)	Farmanguinhos	tuberculostatic	synthetic	30/11/2015	0,10
Sevelamer	Farmanguinhos	hyperphosphatemia	synthetic	18/12/2016	0,33
Tenofovir + Lamivudine (2 em 1)	Farmanguinhos	antiretroviral	antiretroviral	22/12/2015	0,78
Imatinib (Mesylate)	Farmanguinhos	oncological	synthetic	27/12/2013	7,09
Tacrolimus	Farmanguinhos	immunosuppressor	synthetic	16/12/2011	1,63
Trastuzumabe	Tecpar	oncological	biological	04/04/2018	379,32
Infliximab	Biomanguinhos	Rheumatoid artritis	biological	28/11/2014	362,63

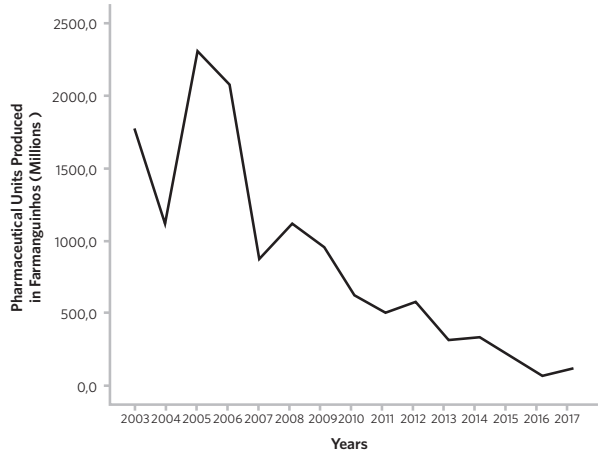
Fonte: Ministério da Saúde[29].

The implementation of PDPs in 2008 found Farmanguinhos in a declining curve in the production of pharmaceutical units, as shown in *figure 1-A*. Between 2003 and 2017, the fall in the production of pharmaceutical units in Farmanguinhos was 21% a year. The highest level in the use of installed capacity happened in 2005 (2 billion and 500 million in pharmaceutical units).

At the beginning of the 2000s, Farmanguinhos maintained the production of lines of technological development and the production of orphan medicines, so called due to the lack of interest in private sector in developing or producing them because of the low prospects of economic return. These are the cases of production for diseases such as tuberculosis, leprosy, malaria, etc.

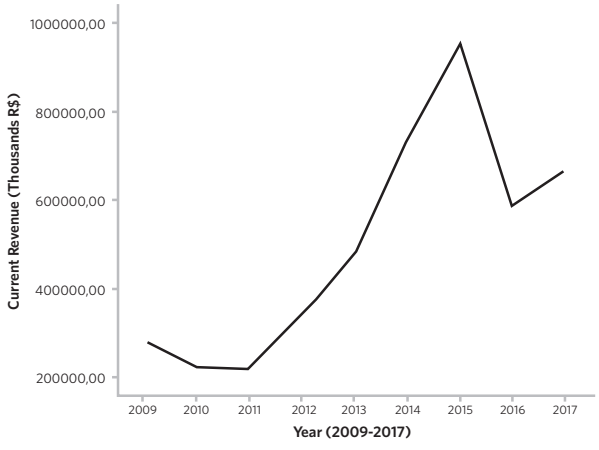
Farmanguinhos also enjoyed a significant position in the production of similar medicine in response to the growth of demand for the Brazilian Family Healthcare Strategy and the treatment of diabetes and privileged access through centralized purchases by the Ministry of Health. This comfortable situation changed abruptly due to the decentralization of the purchases by municipalities from 2005 onwards[30]. The launch of the Popular Pharmacy Program (PFP) in 2004[31] did not modify this critical scenario , as its demands to Farmanguinhos was barely significant, as shown below. Moreover, in 2003, Farmanguinhos lost the monopoly of the supply of antiretrovirals to the Ministry of Health due to the entrance of public laboratories, especially Lafepe, as well as the entrance of new medicines in the DST/Aids program[23].

Figure 1-A. Production of Pharmaceutical Units in Farmanguinhos: 2003-2017



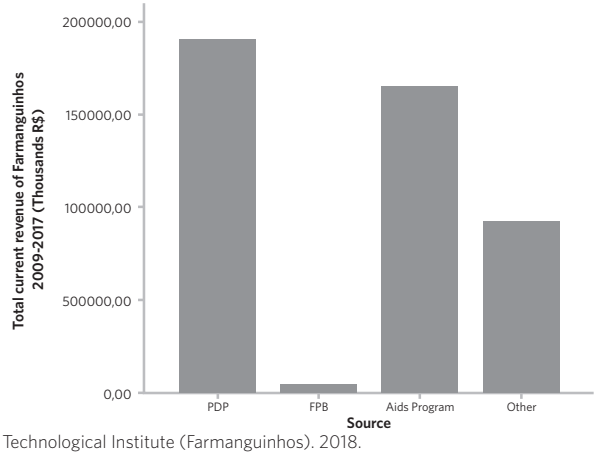
Source: Fiocruz Administrative Reports – 2003-2017.

Figure 1-B. Current revenue of Farmanguinhos – 2009-2017 (in thousands of R$)



Source: Board of the Pharmaceutical Technological Institute (Farmanguinhos). 2018.

Figure 1-C. Distribution of Farmanguinhos' sources of revenue – 2009-2017



Source: Pharmaceutical Technological Institute (Farmanguinhos). 2018.

Given this scenario of declining productivity, it is no surprise that the Brazilian General Office for Controllership (the CGU) questioned that the production numbers were too low as only 66 million pharmaceutical units in 2016, which represented the use of only 1% of the operational capacity of the Medicine Technological Complex (Complexo Tecnológico de Medicamentos – CTM), its factory facility acquired in 2004 (https://auditoria.cgu.gov.br/download/10000.pdf. Consulted on 16/01/2019)[32], as *figure 1-A* shows.

According to the CGU audit reports,

> The principal reasons which specifically explain the fall in production in 2016 are the following: a) Reduction in Ministry of Health demand for medicines in the DST/Aids Program manufactured by Farmanguinhos, specifically Efavirenz and Lamivudine + Zidovudine, which are those with the highest volume; b) Replacement of the production of Lamivudine by the acquisition of Tenofovir + Lamivudine from the laboratory Blanver Farmoquímica Ltda, its private partner in the Partnership for Productive Development (PDP); c) Impossibility of the supply of Amoxicillin, suspended by Anvisa [...]. In this way, in absolute terms, the principal explanation of the minimum production in 2016 was the fall in demand on the part of the Ministry of Health for medicine from Farmanguinhos' portfolio. It is worth noting that the strategy adopted by Farmanguinhos to return to production, with medicine from thirteen Partnerships for Productive Development (PDPs), has still not produced results[32].

However, the conclusions of the CGU should be assimilated cautiously. It is important to bear in mind that the effect of PDPs on the productive structure of Farmanguinhos could not be completely assessed because the cycle of technological transfers of projects was not concluded. Not mentioned by the CGU is the fact that conducting the medicine purchase processes linked to the technological transfer of PDPs allowed significant increase in the unit's revenue from 2011, reversing the trend of the previous two-year period, as shown in *figure 1-B*. The definition of revenue in *Figure 1-B* considers the sum of sales of medicines from the traditional portfolio and the funds allocated to the unit for the acquisition of medicines and technology transfers under PDPs through decentralized funding. In 2015, the peak of the historical series, the unit's revenue was R$990 million (current value).

Figure 1-C demonstrates that the contribution of the PFP to Farmanguinhos' revenue in the period 2009-2017 was insignificant. The winners with the PFP were the most important generic medicines producers[31]. Actually most of Farmanguinhos' revenue still comes from the STD/Aids program and medicine with a traditional portfolio (not covered by PDPs). However, the important share of PDPs may indicate that Farmanguinhos can expand its scale of production, under the constraint of the monopsony exercised by the Ministry of Health.

Final considerations

Lall[33] highlights the importance of the demand function in the configuration of technological aptitudes of organizations as it affects not only product development, administration quality, marketing practices, but also the scale and scope of production. According to him, companies submit themselves to a costly, uncertain, prolonged, and unpredictable learning, even when the technologies in question are well known.

For this reason, due to the economy of scale inherent in many industrial activities, the incentive for competitive largescale companies to conform can also be an option to reduce uncertainty about technological adaptation technology[33]. The article demonstrates that this was not the path chosen for PDPs. The federal government's choice of deconcentrated

high-cost medicine acquisition paradoxically affected the sustainability of the largest LFO owned by the central government.

The article shows that the technological internalization proposed by the innovative PDP agenda for LFOs can result in events not anticipated by conventional knowledge. It was assumed that organizations are moved by specific technological trajectories in which previous learning leads in a determined adaptive direction. Once adopted, the technological trajectory is difficult to change and sunk costs tend to persist for a long period[32].

Due to the unused organizational capacity within Farmanguinhos, the elevated dispersal of the distribution of local production of strategic medicine under PDP among state and federal laboratories did not favor an increase in the efficiency and diversification of the Fiocruz's scope. Concerning Farmanguinhos, the efficient use of the elevated productive capacity installed – gaining scale – requires a substantial part of government demands generated by PDPs to be concentrated in it. This is not what happened.

The spread of the purchase process acted as an isomorphic force over the LFOs. PDPs not only decide the technological incorporation strategy but also the conditions of supply due to the single purchaser function of the Ministry of Health, with no alternative being presented to the LFOs searching for other markets.

Regarding scope, this article shows that PDPs favored the incorporation of biological medicines for some LFOs, allowing the offer of multi-products and the creation of a singular technological route. This is the exemplary case of Bio-Manguinhos, which during the development of the PDP policy changed from a laboratory specialized in a single product (vaccines) to the production of biological medicines with more mature medicines. The adaptive skills observed in Farmanguinhos did not allow a transition to a new technological route of multi-products, despite the increase in complexity and price of the medicine incorporated in the portfolio as a result of PDPs.

Given this scenario, in this article we identified that the immediate further challenge for Farmanguinhos is the management of its elevated lack of organization capacity caused by the Ministry of Health's purchase model under PDPs. This path can open space for the reduction of the high dependence on centralized purchases by the Ministry of Health and enable the exploration of new markets.

Collaborators

Costa NR (0000-0002-8360-4832)* contributed to the conception, planning, analysis, interpretation of data, and final approval of the manuscript. The authors Lago RF (0000-0002-5130-7411)*, Sousa ACA (0000-0002-5288-2274)*, Raupp AC (0000-0002-3893-7056)*, and Jatobá A (0000-0002-7059-6546)* contributed equally to the drafting of the manuscript. ■

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