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On Sanitary Sovereignty in the Health Industrial Complex

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Abstract *The article discusses the place of the Health Industrial Complex in the government initiative for a new industrialization in Brazil. To this end, it discusses possible paths that the initiative reserves for its various components. It begins by discussing the appropriateness of this process to target "sanitary sovereignty" as an objective. Then, it points out the necessary articulation of the health industry with the general industrialization policy. It emphasizes the role of the State and the private sector in this process and emphasizes the presence of the SUS and the Ministry of Health. Finally, it points out the conditions of competition between the Health Industrial Complex and the global industrial oligopoly.*

Key words *New industrial policy, Health Industrial Complex, Science, Technology and Innovation in health*

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Sovereignty and the right to rule cannot be conferred on anyone no matter who... as a result of an academic discussion. Sovereignty is acquired by force and power and violence.
Mustafa Kemal Ataturk

About the use of the concept of Sovereignty in the health context

Regarding the concept of sovereignty, it is worth mentioning that it belongs to the field of political science, geopolitics and its executive tool, diplomacy. It concerns the place of the state as the highest point in a hierarchy of power within its borders. As it is used today, this concept was exalted from 1648 in the so-called Peace of Westphalia. There, the borders of many European national states were established and the concept of the Nation-State was inaugurated. From then on, every time war was declared or peace was negotiated, the issue of national borders came to the fore. The principle of inviolability of national borders was part of the League of Nations and, after World War II, of the UN Charter. In both cases, this principle was present despite the fact that they were violated dozens of times around the world. And in the face of violations, the most common result is war. This comment aims to moderate the use of the term when discussing the degree of self-determination of a country within the scope of the Health Industrial Complex.

In the health context, sovereignty is established in the Federal Constitution of 1988 in Articles 196 and immediately following. These devices define human health as a right, based on the notion of universality. It is a provision that, conceptually, does not admit a greater or lesser degree: all citizens have the right to health and the guarantee of this right is a duty of the Brazilian State. However, in the specific context of the Health Industrial Complex (CIS) we have a different situation, in which the difficulties currently posed to it relate more to the notion of self-sufficiency than sovereignty. There are no countries that are 100% self-sufficient - therefore sovereign - in the CIS field. For example, the drug market in the United States of America, world leader in the health industry, is around US$ 700 billion annually[1] and that country imports something like US$ 165 billion in API's and finished drugs[2] – an important self-sufficiency, but not sovereignty.

There are huge inequalities in the degree of self-sufficiency between countries. One of the first steps towards increasing inequality was the enactment of the TRIPS agreements, in 1994 at the WTO, which "harmonized" the rules on intellectual property worldwide for the benefit of the countries that own patents. More recently, with the crisis of productive and financial globalization and the displacement of the geopolitical axis to the East, the collapse of the utopia of free, deregulated and complementary markets has also contributed to the increase in this inequality. During the COVID-19 pandemic, this process was radicalized and became evident in the field of vaccines. The 2022 WHO vaccine report shows that of all vaccines against SARS-CoV-2, only 14% came from its COVAX initiative, aimed to reach poor countries[3]. It is important to emphasize that the occurrence of the pandemic did not originate this phenomenon, but expressed it more acutely.

The Health Complex is not an island

Currently, the manufacturing industry in Brazil accounts for about 10% of the Gross Domestic Product and in the mid-1980s it accounted for almost 30%. The process of de-industrialization in national economies was not an exclusively Brazilian phenomenon, but in our country it had particularly harmful characteristics, both due to the structural characteristics of the formation of the industrial park (import substitution without mastering the technologies involved) and to the revolution in standards of industrial production operated in leading countries during our path of deindustrialization, based on the incorporation of advanced technologies in production processes (industry 4.0). Currently, when a new attempt to reindustrialize the country is being rehearsed, it is essential to warn that the CIS is not an island and its strengthening with a view to increasing our health self-sufficiency will require articulation with the general effort of this new attempt.

Claiming a priority position for the CIS among other industrial sectors stems not only from its social relevance, but also from its economic and strategic impact. On an economic level, because the CIS brings together a large contingent of workforce with highly qualified components. At the strategic level, because it is intensive in technology and, alongside with the information and communication technologies industry, it is the one that invests the most in technological development. The starting point of this new process of stagnating deindustrialization was the reactivation of the National Council for Industrial Development (CNDI), linked to

the Presidency of the Republic[4]. Its work proposal encompasses seven priority missions, each one under the responsibility of a working group. The CIS is represented in a mission called "Resilient health complex for the prevention and treatment of diseases"[5].

The industrial production chain of medicines currently encompasses four types of industries: pharmochemical industry; chemical-based pharmaceutical industry; biotechnology-based pharmaceutical industry (including vaccines); pharmaceutical industry of natural products. Although they are all part of the same Complex (CIS), they have very particular characteristics. These differences lie in the fields of production scale, the technologies involved, the production processes, the added values, the weight of each one in the global market and the trends projected by each one in this market. Therefore, existing bottlenecks and ways to overcome them must take these specificities into account, and a debate on increasing self-sufficiency must take these differences into account.

The pharmochemical industry's main input is synthesis intermediates, most of them derived from the petrochemical industry (benzene, ethanol, ethylene, etc.) subjected to various transformations. In the pharmaceutical field, these transformations result in active pharmaceutical ingredients (IFAS), the basis of drug composition. IFAS represent a relatively small proportion of the finished drug cost. It follows that its production scale is an essential variable to estimate the success of a productive unit in this industry. Many IFAS are considered commodities. However, the market for more complex chemical-based drugs increasingly demands APIs with greater added value, which are not considered commodities and this fact is important in the formulation of an industrial policy for this segment. We currently import around 95% of IFAS for medicines produced in Brazil[6]. In the 1980s, we imported around 50% (other estimates say 20%). The change was due to the commercial opening that occurred in the 1990s. This opening led to the closure of many IFAS production units in the country, which could not compete with Indian and Chinese production, anchored in stricter industrial policies in the sense of stimulating the local production.

Currently, it is unlikely that a local production of pharmochemicals based on commodities can be competitive with India and China due to the differences in production scale, the lower cost of labor in those countries and the hegemony they have conquered in the major world markets. The strategy for the local industry must be directed towards selected, more complex molecules and to encourage public purchases. However, the existence of shortages of essential medicines in Brazil suggests that more traditional molecules, such as antibiotics and other products present in shortages, are also prioritized. Recently, the Brazilian Association of Fine Chemistry (ABIQUIFI) handed over to the Ministries of Health and Science, Technology and Innovation a study with measures for the increase from 5% to 20% in pharmaceutical ingredients produced in the country. In a similar trajectory, Fiocruz and the Association of Fine Chemicals, Biotechnology and Specialties Industries (ABIFINA) signed an agreement for the joint elaboration of a set of IFAS considered strategic for the public Unified Health System (SUS)[7]. A detailed view of the challenges and opportunities of the Brazilian pharmochemical industry can be found in the work "Are there competitive spaces for the Brazilian pharmochemical industry? Reflections and proposals for public policies"[8].

The Brazilian drug market is worth around US$ 25 billion and retail sales represent around 70% of it; 30% are institutional sales, including SUS purchases. Differently from pharmochemicals, the pharmaceutical industry based on chemical synthesis showed great growth and consolidation after the opening of trade in the 1990s. Policies encouraging generics, sustained increases in the minimum wage, Popular Pharmacy programs and the Productive Development Policy, which will be mentioned later were responsible for that. Currently, among the 18 largest pharmaceutical companies operating in Brazil, ten (among which the largest) are national capital companies[9]. About 80% of the medicines consumed in the country are manufactured here in whole or in part. Among the drugs wholly manufactured here, the leading companies in the market are those with national capital and their market share is the majority in terms of pharmaceutical units. In terms of value, multinational companies with factories or offices in Brazil hold the largest market share. Multinational companies headquartered in Brazil have been deactivating production units since the opening of trade in the 1990s. They are increasingly importing finished drugs, only packaged in Brazil.

The Association of Official Laboratories of Brazil (ALFOB) encompasses 21 active laboratories, the majority public (10 federal and state owned) and the others with different legal status.

This network has very heterogeneous degrees of productive and technology absorption capabilities. Among the official laboratories, those that produce immunizers stand out – vaccines and serums. They are the Institute of Technology in Immunobiologicals (BioManguinhos/Fiocruz), the Butantan Institute, linked to the government of São Paulo state and the Institute of Molecular Biology of Paraná (IBMP), managed by a consortium between Fiocruz and the Institute of Technology of Paraná (TECPAR). Mention should also be made of the Ezequiel Dias Foundation (FUNED), from Minas Gerais and the Ataulpho de Paiva Foundation, currently in the process of being associated with Fiocruz. These institutions play an important role in a policy for the CIS because, although they are highly heterogeneous in terms of their portfolios and their technological/productive capabilities, their relevance resides in their performance guided 100% by the close link they have with SUS.

The world has witnessed great advances in the field of technologies for the production of drugs by biotechnological routes. Despite the fact that they currently represent little less than 30% of the world drug market, everything indicates that the future of the pharmaceutical industry is to become a biopharmaceutical industry. Parallel to this trend, the vaccine industry, which today is organically integrated with the drug industry and accounts for just under 10% of the world drug market, follows that trend. Currently, exploring a whole new universe of vaccines based on platforms of different types, as seen in the COVID-19 pandemic.

In addition to proximity to the SUS, the official laboratories that develop and produce vaccines and biotechnological drugs have been preparing to adjust to these new global trends. BioManguinhos, Butantan, FUNED and IBMP, through different choices in terms of targets, greatly increase their strategic importance for increasing health self-sufficiency, given their technological and productive experience.

Currently, both Butantan and BioManguinhos dominate the more traditional technologies and the most important challenge in this regard is the technological and productive mastery of the new platforms for biomedicines and vaccines. Historically, both institutions, in most of their successes, have based their activity on a technology transfer strategy through voluntary licensing. In addition to the international prestige of both, the great demand of the SUS National Immunization Program made it attractive for technology holders to negotiate the transfer with some technological compensation clauses, which provided a good part of their training in this field. However, this important mechanism presents several and already known difficulties, in addition to an exhaustion that tends to grow with the technological innovations now observed in the field of vaccines and biomedicines. The traditional problems in this strategy are, among others, the possibility of transferring obsolete technologies whenever the contract does not provide for updates, and the non-transfer of all technology, leaving the recipient in permanent subordination to the seller, as well as the limitation of markets and prices for the locally produced product. The reason for the probable future narrowing of this path is that new technologies based on new platforms, in many cases, will not be for sale as compensation for the purchase of finished products by SUS. Not just for commercial reasons, but also for the technical difficulties involved in an eventual transfer. Hence the need to explore new forms of association, such as risk sharing agreements, already successfully tested in the case of the respective vaccines during the pandemic.

As already noted above, the current geopolitical framework and the COVID-19 pandemic have generated a break in many global production chains that were previously shared and complementary to some degree. All over the world, this break had as a clear result the need to introduce, in some sectoral policies, the incorporation in the country of upstream stages in the technological and productive processes related to these policies. With regard to the CIS, this incorporation is unquestionable and there are news in Brazil of products in the development process from the bench. Without intending to be exhaustive, projects of this nature are underway at USP, UFMG and Fiocruz. The speed and conditions of success of these initiatives depends on a great increase in support for basic and translational scientific research.

Among the bioproducts of strategic interest to the country are those derived from human blood. Particularly in crisis situations, but not only, complete mastery of the collection, purification, fractionation and production of blood products is essential. Hemotherapy in Brazil has been built on public and universal bases, and great steps have been taken towards the supply of blood and its fractions to the public. This was achieved through the installation of 36 blood centers and coordination bodies throughout the country[10]. Also noteworthy is the NAT KIT for

detecting HIV and Hepatitis B and C in blood bags, fully developed at IBMP and introduced in the network since 2011 by Bio Manguinhos. Recently (2022) the NATplus KIT was launched, which added malaria to the previous targets. However, mastering the complete cycle in handling human blood is still a challenge in Brazil. After long setbacks, the Hemobrás industrial plant in Goiana, Pernambuco State, is being reactivated with a view to its conclusion. Technological training is still being carried out through technology transfer and the challenge to be overcome is the complete mastery of recombinant technologies and the indigenous production of the main blood products.

In 2015, there were 166 companies with active licenses in the natural products pharmaceutical industry segment. Its market is predominantly domestic. The current trend is for a decrease in the number of companies and new licenses. This reduction in the number of companies has been carried out in favor of companies with foreign capital. In the largest companies active in herbal medicines, this is not the main activity. Despite the great Brazilian biodiversity, the sector suffers from low standardization of raw materials and regulatory difficulties in accessing their sources. The natural products industry has very little articulation with the SUS, although the topic of natural medicines is quite traditional[11].

The role of the National State and SUS in the Health Complex and the competition conditions

A new level in the scenario of self-sufficiency of the CIS will have to be reached with the concurrence of multiple actors, public and private. The advancement of the New Industrial Policy, which, as already mentioned, has the CIS as one of its priority sectors, places the private industrial park as an indispensable actor. The new industrial policy should have a specific look at each of the components of the CIS, whose demands are different. Pharmochemicals, medicines, medical therapeutic and diagnostic devices, materials and other components of the CIS, each of these industries will need to be the object of a different look. However, this does not exempt it from pointing out a dimension that constitutes a challenge common to the entire Brazilian private industry in the sanitary field and that will require a concerted action between this industry and the public power. This dimension is the gigantic economic-financial power and the lobbying power of the international sanitary industrial oligopolies. These oligopolies have increasingly projected their power into public policies in the world's major markets, including the countries where their headquarters are located. Currently, the US government is waging a real war with the pharmaceutical industry, which is mostly based in that country, related to rising prices[12,13]. Similarly, in Europe there is currently an intense tussle between governments and industry over prices[14].

The difficulty of such powerful governments in facing competition with the so-called "Big Pharma" essentially stems from this enormous power that controls a global market of US$ 1.5 trillion[15]. And where, in 2021, the 10 largest pharmaceutical companies accounted for 1/3 of that market and the 20 largest for almost 50%[16]. But the scenario of concentration does not occur only in medicines. With regard to diagnostic equipment (imaging and others), the concentration is corresponding, with the ten largest companies accounting for 38% of the world market in 2021[16]. A reindustrialization policy in a peripheral country that, despite having a large internal market, can compete in this highly concentrated scenario, requires a virtuous articulation between the private sector and the State, the latter being the key piece of strategic guidance and financial support.

The exercise of power by these oligopolies, particularly in the pharmaceutical field, takes place mainly within the scope of national intellectual property policies and this has been intensifying since 1994 when the TRIPS agreements, mentioned at the beginning of this text, entered into force. There will not be an adequate industrial policy in the sanitary field if the Brazilian intellectual property (IP) policy is not taken into account. In Brazil, this policy presents important challenges both in the instance that elaborates it and in the one that executes it.

Countries that have industrialized more recently (Japan, Korea, India, China), without exception, locate the formulation of their IP policies in the highest instances of political power. In Korea, for example, the committee that formulates policy is chaired by the President of the Republic, and in Japan by the Prime Minister. This does not occur in Brazil, where this formulation is attributed to a collegiate of low political hierarchy located in the Ministry of Development, Industry and Foreign Trade – the Interministerial Group of Intellectual Property (GIPI). In addition to this low hierarchy, GIPI has been directly and indirectly penetrated by oligopoly interests,

through law firms on its behalf. A new configuration of the IP policy-making body would greatly help a new industrial policy for the CIS.

On the policy execution side, whose responsibility lies with the National Institute of Industrial Property (INPI), the problems are located in the progressive weakening of the agency, due to the loss of qualified personnel and difficulties in the use by the INPI of the financial resources arising from its revenues that impede its institutional strengthening. A recent important step towards changing the IP scenario in the health field was the declaration, by the Federal Supreme Court (ADI 5529), of the unconstitutionality of the Sole Paragravaccine and sera ph of Article 40 of the Brazilian IP Law, which allowed the undue extension of the period of protection patent beyond the regular 20 years.

In the health field, the strategic orientation of the industrial policy implies placing at the service of strengthening the CIS the instance that acquires around 25% of the medicine market, something around 50% of the equipment market and over 90% of the vaccines and sera markets. This instance is the SUS, which has among its main priorities the expansion of access to CIS products by the population. Financial support, in addition to the companies' own investments, must rely on the work of the network of federal and state agencies operating in the field of science, technology and innovation, namely BNDES, Finep, Embrapii and state development agencies.

The articulation between the SUS, through its federal manager, and these agencies will not be an original initiative, given the accumulated experience of 15 years of implementing the Productive Development Policy in the Ministry of Health, through the contracting of public-private partnerships that could attract the pharmaceutical industry private sector and official laboratories for the development and production of important items for public health, saving resources and expanding access to these items (Partnerships for Productive Development). This policy, despite its largely positive balance, must be revisited with a view to overcoming some weaknesses. Among them, it is worth mentioning the heterogeneity of some official laboratories regarding their ability to absorb the technologies involved in product development. Another important point that deserves attention is the review of the processes for choosing products to be included in the policy, which often involved mature technologies or those at the end of their cycle, which resulted in extending their patent protection period. It is also worth mentioning the need, in the process of defining candidate products for the partnerships, for there to be a greater balance between the choice of more expensive and complex products and more traditional products that have been subject to a shortage of supply in the domestic market. And, finally, include in the policy mechanisms for technological ordering (with risk sharing) for products whose development is still in the proof-of-concept or pre-clinical or clinical trials phase.

The Productive Development Policy focused its activities on medicines and vaccines, which was a correct choice. But it will be important to extend it to the field of therapeutic and diagnostic equipment and materials of lower added value which, as the recent pandemic has dramatically shown, can assume a very great importance.

It is known the weight that expenses with the purchase of health products and services have on the economy of families, even with the existence of universal public health systems. Even more so in countries that do not have health systems of this type. For the poorest families, out-of-pocket expenses with medication are the main item of direct expenses, which can lead to catastrophic situations when out of control. For this reason, price regulation, in addition to mitigating excessive spending on medicines by families and the SUS and expanding access to them, has an indirect economic meaning, which is to prevent higher health expenditures in the care of aggravated problems for not using medicines and other products at the right time. In the year 2000 there was a Parliamentary Commission of Inquiry on medicines that introduced price controls in the country. As a result of incremental improvements, notably the creation of the Medicines Price Regulation Chamber (CMED) in 2003, this control policy maintained significant price stability[17].

The most notable fact is that CMED's action has not prevented the excellent performance of the pharmaceutical industry in Brazil since its creation, as presented in the previous section of this text. Therefore, the existence of the CMED and price controls, contrary to what one might think, was not a weakening factor for the CIS. This comment is important because recently (2022) there was an attempt to move the CMED – an eminently sanitary tool – from the sphere of the Ministry of Health, where its executive secretary (Anvisa) is located, to the Ministry of Economy (currently Ministry of Finance). An-

other attack whose result, if implemented, would be to weaken price controls, also from 2022, was the claim for differentiated (and higher) pricing for product launches that featured 'incremental innovations'. Souza *et al.*[18]. list arguments that demonstrate that the relationship between price increases and incentives for innovation is much more complex than a direct linear relationship. In addition, the proposal speaks of 'incremental innovations', whose categorization is too broad, diffuse and therefore inappropriate to guide pricing.

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