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Policies for fostering health science, technology and innovation in Brazil and the role of clinical research

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Abstract *The purpose of this article is to highlight a number of underlying issues that may be useful for a comprehensive review of the management of Health-Related Science, Technology and Innovation policies (ST&I/H), and its strategies and priorities. It is an analytical study supported by an extensive review of the technical and journalistic literature, clippings, legislation and federal government directives. The results show that the Healthcare Production Complex undeniably and increasingly needs science to maintain itself. One may infer that a framework of institutional milestones is being built in Brazil, to strengthen, guide and encourage Research and Development, and that clinical research creates scientific knowledge to address public healthcare issues by generating new inputs or enhancing existing techniques, processes and technologies that will be produced, marketed and used in the different segments, thus feeding the Healthcare Productive Complex.*

Key words *Policies, Healthcare administration and planning, Management of science, Technology and innovation in health, Clinical trials*

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Introduction

This study addresses the structure of the SNIS (NHIS) - the National Healthcare Innovation System - as the interface with SUS, the Unified Healthcare System, as this connection is an important social and economic element for the country.

To understand clinical studies as a window of opportunity to foster innovation, one must first introduce the historical context in which the Department of Science and Technology (Decit) was created within the Ministry of Health. A number of concepts were defined wit this in mind, and also considering that this structure, as the formal structure to promote different relevant activities - research, knowledge dissemination, and product and process development -, interacts and creates links that provide specific knowledge and competence, in search of an effectively innovative performance[1].

We designed a framework that promotes the sustainability of Science, Technology and Innovation (ST&I) and regulation in Brazil, along with the public policies to strengthen it. It also fosters windows of opportunity crated from network arrangements provided by clinical research - one of the strategies to produce healthcare goods and services.

Its purpose is to highlight a number of underlying issues that may be useful for a comprehensive review the theme to manage health-related Science, Technology and Innovation policies (ST&I/H), and its strategies and priorities.

Regarding the approach to network possibilities, links and collaborations, we reveal the main players in creating measures that support processes. We also present potential arrangements of the players in the National Network of Clinical Research, showing the elements to consider when designing partnerships that will foster and strengthen ST&I/H in Brazil.

This is an analytical paper supported on an extensive review of domestic and international literature related to the tools and policies used to strengthen science, technology and innovation in health in Brazil. We performed non-systematic searches for articles and dissertations in the main scientific databases, in addition to the so-called "grey literature". Other sources of data included book chapters, technical and journalistic texts, legislation and federal government directives. This article is a segment of the Ph.D. dissertation of the main author, entitled "Managing networks for scientific, technological and innovation in healthcare in Brazil".

National System for Innovation in Healthcare

In the late 1980s the concept of a National Innovation System (NIS) first emerged in studies by Freeman[2], to explain the economic performance of Japan at that time. This a set of diverse institutions focused on generating, incorporating, using and disclosing knowledge sourced from companies, organizations and other institutions involved in the process[2]. This is also explored to explain how knowledge and innovation determine national competitiveness, especially as this new concept extrapolates the individual focus when associated with organizational analysis. The studies of Freeman[2], Lundvall[3], and Nelson[4], in Costa[5] are considered the origin of this concept.

The process leading up to the National Health Innovation System in Brazil included in particular the development of a theoretical framework from which derives the concept for the Economic-Industrial Healthcare Complex[6,7]. This in turn is based on a social-development project, enabling articulation between social inclusion, mass consumption, increased jobs and income, a stronger manufacturing structure, and innovative processes and investments, potentially reducing nation's dependence, which according to Costa[5]:

...the political-institutional framework of the Economic-Industrial Healthcare Complex is influenced by the activity of the State (relationships of power, decision-making structures and formulation of implicit and explicit policies), institutions (from formal education and S&T institutions, to development and funding agencies, for example all the way to standards of conduct embedded in society), an organized civil society (associations for example), and the population in general.

It is clear that innovation in healthcare involves a field of excellence, given that it is able to mobilize the ST&I/H infrastructure and articulate with the industrial base to promote its consolidation. Furthermore, it is seen as a political and social process, as it is part of the nation's strategic planning, focused on reducing the its dependence on health-related inputs manufactured abroad, reinforcing the nation's economic policy[8,9].

Policies and actions: development of the regulatory framework and Science and Technology incentives

Among the instruments and policies designed to support ST&I/H measures, one should highlight the National Policy for Science, Technology

and Innovation in Health, and its articulation with the National Healthcare Policy and the National Science, Technology and Innovation Policy. We understand that their guiding principles and strategies are tools to facilitate the interface between the State, the market and the scientific community on behalf of the Unified Healthcare System (SUS)[10,11].

The National Agenda of Healthcare Research Priorities (ANPPS) includes one of the National Policy for SC&I strategies, and takes on the important role of guiding measures to foster research and training of human resources for the SUS, enabling efforts on behalf of areas that are actually a part of the strategic elements that address public healthcare problems at the local and national level.

The development of the National Agenda of Healthcare Research Priorities had the ample support of the scientific community, healthcare managers and social control representatives in Health, Education, Science & Technology and Social Services. A number of city, state, regional and national seminars were held as part of this process, culminating in the 2nd National Conference on Science, Technology and Innovation in Healthcare (CNCTIS) in 2004[12-14].

The National Conference on ST&I/H became a political-democratic tool, considering the following elements of how and why it was created: i) the healthcare situation and life conditions of the Brazilian population - systematized in the publication entitled *Saúde no Brasil: Contribuições para a Agenda de Prioridades de Pesquisa* (Healthcare in Brazil: contributions to the Agenda of Research Priorities); ii) the definition of sub-agendas in research, created by a Technical Advisory Committee made up of experts and managers; iii) the definition of research themes listed by working groups for discussion in each sub-agenda[10,13].

Thus, the National Agenda of Healthcare Research Priorities and the National Policy for ST&I/H are the guiding instruments for ST&I/H measures within the Ministry of Health Department of Science, Technology and Strategic Inputs (SCTIE).

Another initiative that has contributed to positive changes in S&T in Brazil was the creation of Sector Funds in 1999, under the management of FINEP, the agency that funds studies and projects, part of the Ministry of Science, Technology and Innovation. This venture picked up pace when a set of tools, policies, programs and laws favorable to the National Innovation System came into effect[15].

Chart 1 is a chronology of the main tools and policies that contributed to a more robust ST&I/H, and are strong allies in fostering innovation in healthcare.

The instruments in the chronology are not exhaustive. Numerous other instruments, for example terms of cooperation signed by the MoH and MST&I have enabled and facilitated the implementation of a set of measures that favor, strengthen and collaborate to intensify the demand for R&D/H and ST&I/H, promoting greater reliability for the players involved in generating products and processes - universities, research centers and public and state-owned companies -, along with investors and consumers[16].

This analysis shows that a framework of institutional milestones is being created in Brazil to strengthen, guide and incentivize R&D/H and ST&I/H activities in the country, and also to articulate with the incentives of the productive sector. However, it is also important to point out the increment in S&T provided by the CNPq, the National Council for Scientific and Technological Development starting in the 1950s, by Fapesp, the state of São Paulo Foundation for Research Support created in 1962, and by Finep, which since 1971 has funded studies and projects[17].

Real articulation between the players across these policies may facilitate access to results, attract foreign S&T for innovation in Brazil, and provide the State with tools to respond to increasing social and market pressure to incorporate high-value added, high-technology products into SUS[16].

Department of Science and Technology and Research Promotion

At the federal level, responsibility for fostering, monitoring and assessing health research projects are the prerogative of the Department of Science and Technology, part of the Department of Science, Technology and Strategic Inputs (SCTIE) of the MoH. This is the main agent in charge of enforcing the National Policy for ST&I/H, promoting inter-sector articulation of the National System for Science and Technology in Healthcare.

Following the 2nd National Conference on ST&I/H, which approved the PNCTIS and National Agenda of Healthcare Research Priorities, the Department of Science and Technology became the main player in fostering R&D in the area of health in Brazil, incorporating an important differential compared to the previous model

Chart 1. Breakdown of the main political tools related to scientific development, research, training in science and technology and innovation. Listed in chronological order.

Year	Instrument	Comment
1990	**Law 8,080/1990 (Art. 15 § XIX)**	Defines that it is the responsibility of SUS to foster research and studies in health-related areas.
1994	**1st CNCTIS**	1st National Conference on Science, Technology and Innovation in Health - promoted the institutionalization of the political debate of SUS responsibilities in fostering R&D/H.
1999	**Sector Funds**	Funding for research, development and innovation projects. The Healthcare area is responsible for: CT-Health, CT-Infrastructure, CT-Biotechnology, CT-Green/Yellow, and for all cross-sectional activities involving more than one fund.
2001	**Millennium Institute Programs**	Stimulates the development of inter-laboratory research networks to capture all of the potential of the existing physical infrastructure.
2004	**2nd CNCTIS**	2nd National Conference on Science, Technology and Innovation in Health - brought together the goals of the National Healthcare Policy and those of the National Policy for Science and Technology, increasing the interaction between Health, Education, Science and Technology.
	PNCTIS	National Policy for Science, Technology and Innovation in Health - defines that national development in ST&I/H proceed sustainably, supported on the production of technical and scientific knowledge adjusted to the economic, social, cultural and political needs of the country.
	ANPPS	The National Agenda of Healthcare Research Priorities guides the research priorities to be promoted, according to the principles of the unified system (SUS).
	Law 10,973/20204 - Innovation Law	Defines measures to incentivize ST&I within the productive environment for developing capabilities and enabling the country to achieve technological and industrial development autonomy.
	PITCE	The National Policy for Industry, Technology and Foreign Trade defines innovation as a core dimension of the manufacturing and foreign trade policy.
	Law 11,105/2004 Biosafety Law	Sets safety guidelines and defines mechanisms to oversee activities involving Genetically Modified Organisms (GMO) and their derivatives.
2005	**Law 11,196/2005 "Lei do Bem" (Law of the Good)**	Provides tax incentives for technological innovation.
2006	**Economic Subvention Program**	Fosters innovation and increased competition among the nation's companies and its economy.
2007	**PACTI (2007- 2010)**	Action Plan for Science, Technology and Innovation, sought to increase scientific and technological production in the country.
2008	**PDP**	**Production Development Policy -** improves the various sectors of Economic Industrial Complex, including partnerships between businesses and universities.
	GM/MS Directive 1,942/2008 GECIS	Created the Industrial Healthcare Complex Executive Group to implement the Brazilian framework governing strategies to strengthen the CEIS, the Production and Innovation in Healthcare Complex.
	INCT Program	Program of the National Institutes for Science and Technology. 82 INCT in health-related areas, out of 252 incentivized in 2016.
	GM/MS Directive 978/2008	Selects the projects that are strategic for SUS. Prioritizes promotion of RD&I and the manufacture of vaccines, blood derivatives and products for neglected diseases.
2009	**PNGTS**	The National Policy for Technology Management in Healthcare promotes management activities related to the assessment, incorporation, disclosure, management, use and withdrawal of technologies within the healthcare system.
	Law 12,101/2009 Proadi - SUS	Created the Program to Support the Institutional Development of SUS (Proadi - SUS), supporting research strategic for SUS with tax exemption funds. This includes the Hospitals of Excellence program.

it continues

Chart 1. continuation

Year	Instrument	Comment
2010	**Law 12,349;2010 - Government Purchases Law**	Promotes the replacement of imported manufactured goods and services with domestic ones resulting from technological innovation and development performed in Brazil.
2010	**National Graduate Studies Plan (2011-2020)**	Prioritizes R&D in health-related areas, promotes research combining graduate studies, businesses and society, stimulates university-business partnerships, promotes international cooperation, contributes to strengthening the National Institutes of Science and Technology and the Research, Dissemination and Innovation Centers; promotes a stronger National Network of Clinical Research**.**
2011	**PESS Agenda**	The agenda for Research Strategic to the healthcare System defines the SUS lines of research to meet the strategic goals of the 2012- 2015 Multi-Year Plan.
	The 2011-2014 Greater Brazil Program	Strengthened the manufacturing, innovation and national competitive chains, following the PDP and PITCE lines of action to support, develop and implement business technology portfolios.
	Law 12,401/2012	Created Conitec, the SUS National Committee to Incorporate Technologies. This committed advises the MoH in the incorporation, exclusion or changes in new healthcare technologies within SUS.
2012	**National CTI Strategy for 2012-2015**	Enhanced business innovation and consolidated the National Innovation System.
	GM/MS Directive n°. 4/10	Defined guidelines and criteria for production development partnerships; fostered partnerships between public and private institutions, encouraging technology transfer to Brazil.
	CNS Resolution 466/2012	Governs guidelines and standards of research involving human beings.
	Law 12,715/2012 Pronon and Pronas/ PCD	Created the National Program to Support Oncological Care (Pronon) and the National Program to Support Healthcare for People with Special Needs (Pronas/ PCD), which encourages actions and services developed by private, non-profit entities, associations and foundations in the areas of oncology and people with special needs, using funds coming from Income Tax deductions.

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used by development agencies, in that it involved representatives of the scientific community and market segments, as well as healthcare managers, in the definition of the lines of research to be promoted[18,19].

In 2004, the ceremony for the 2nd CNCTIS, made up of state conferences held in all states except Roraima, Tocantins and Goiás, and 307 regional and city conferences, had 15 thousand participants, including delegates, guests and observers. In addition to approving the National Policy for ST&I/H and the National Agenda of Healthcare Research Priorities, discussions included the need to reflect on the tools available at the time to make the new National Policy for ST&I/H management model operational. The aim was to create a development agency for this purpose[12,20].

Considering this, under the theme "Why have a development agency linked to the Ministry of Health?" professor Reinaldo Guimarães, then the director of Decit, presented a panel that defended the creation of a development agency to effectively help implement and enforce the National Policy for ST&I/H and the National Agenda of Healthcare Research Priorities, ensuring more effective processes. However, there was no consensus to approve the creation of such an agency.

DECIT, the Department of Science and Technology, was created within the Executive Department of the Ministry of Health in 2000, and became part of the Department of Science, Technology and Strategic Inputs when it was created in 2003. In its current structure (Figure 1), it has 61 professionals specialized in the finalistic area of coordination to which it belongs. 30% of these have PhDs, 26% have Master's Degrees, 31% are Specialists and the others have undergraduate degrees in some health or related area.

Within the Department of Science and Technology, promotion became effective and grew thanks to the cooperation agreements signed by the Ministry of Health and the Ministry of Science, Technology and Innovation. This enabled

Chart 1. continuation

Year	Instrument	Comment
2013	**INOVA-SAÚDE (2013-2017)**	This program supports RD&I in public and private institutions working within CEIS, enabling continued funding of projects with the potential of reducing the nation's technological dependence in inputs used for healthcare.
	GM/MS Directive n°. 3,089	Prioritizes scientific and technological development of biomaterials and items related to oncology, non-transmissible chronic diseases, neglected diseases, viral diseases, STDs and AIDS.
	Decree 8.065/2013 § 31	Stipulates that the Department of Science and Technology (Decit) will be involved in formulating, implementing and assessing PNCTIS, based on the requirements of the PNS and within the SUS principles and guidelines; coordinate and execute MoH activities in health-related R&D and promote inter-sector articulation within the National System of Science and Technology.
	GM/MS Directive n°. 2,531/2013	Redefines the list of priority items for SUS investments in R&D and manufacture, and creates the PDP.
	PNPC	National Knowledge Platform Program**,** supports partnerships between businesses and science and technology research institutions in Brazil and abroad for on-demand technology and innovative products, processes or services involving a technological risk.
2015	**CNS Resolution nº. 506/ 2016**	Regulates the accreditation of Research Ethics Committees (REC), which make up the REC/CONEP System and provides other guidelines.
	Constitutional Amendment nº. 85/2015	National S&T Code - amends and adds provisions to the Federal Constitution to update how the activities of Science, Technology and Innovation are handled.
2016	**Law 13,243;2016**	SC&I Legal Framework governing stimulus to scientific development, research, and the development of capabilities in science, technology and innovation.

Fonte: Prepared by the authors based on Iozzi[21], Botelho and Alves [9], Almeida-Andrade[16], Vargas et al.[22].

the transfer of funds from the National Healthcare Fund to the National Fund for the Development of Science and Technology, thus allowing its development agencies - CNPq and Finep, to perform all of the procedures require to contract projects under Decit.

This partnership is often referred to as the "perfect marriage", as the funds invested and projects contracted over the years (2004-2015) would not have been possible without the expertise of these agencies. Decit promotes projects in three ways:

✓ National Promotion: public calls that involve free competition for theme-based research projects, open to any institution in the country.

✓ Decentralized Promotion: multiple-theme based public calls promoted by states, and open only to local institutions. This includes the SUS Research Program (PPSUS), which calls for projects based on local needs and research themes listed by the local scientific community and the State Department of Health. Program management is shared between CNPq and the Research Support Foundations (FAP) in each state. The SUS Research Program has strong appeal among the scientific community, as it helps reduce S&T inequality, historically an issue across the different regions in this country;

✓ Direct Contracting: this is used in response to emergency or specific public health demands, such as the recent contracting of studies to fight the problems caused by the Zika virus.

The Department of Science and Technology contracts research either through contracts and agreements, or by decentralizing resources to

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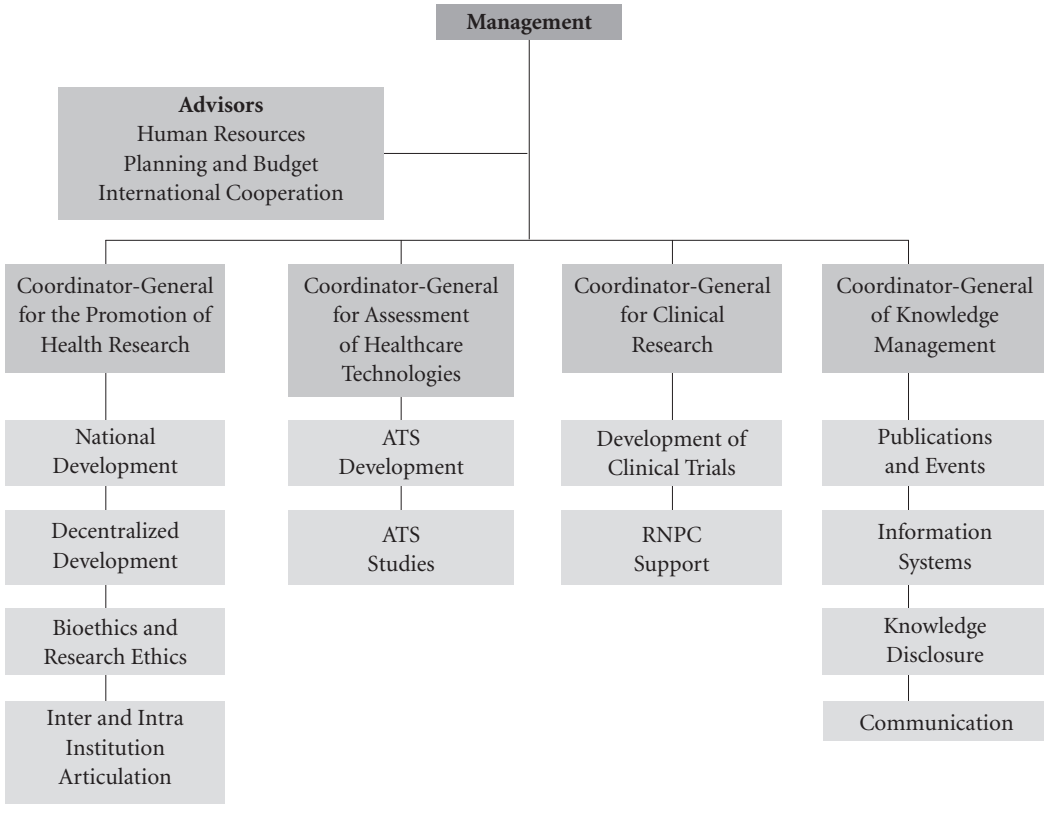


Figure 1. Organization Chart for the Department of Science and Technology (Decit).

Source: The Authors based on documents provided by Decit.

administrative partners. Agreements are operated by the government agreement management system (Gescon and Sincov), and the National Health Fund, or by decentralizing funds in the case of partnerships with MCTI agencies (CNPq and Finep) and Capes (Coordination for the Improvement of University Level Personnel), part of the Ministry of Education, or the state-level Research Support Foundations, by releasing funds to the CNPq, which manages the agreements.

Over the past five years (2011-2015), Decit invested some R$ 509 million in 1,615 research projects, 97% of which were the result of public calls for projects. This investment enabled the expansion and consolidation of the following initiatives: The National network of Clinical Research (RNPC), the Brazilian ATS Network (Rebrats), the National Network for Cell Therapy (RNTC), the National Network of Research in Neglected Diseases (RNPDN), the National Network for Research into Healthcare Policies (RNPPS), the National Network of Research into Cerebral Vascular Diseases (RNPAVC), the National Network of Clinical Research in Cancer (RNPCC), and the National Network for Research in Cardiovascular Diseases (RNPDC). It also fostered technical cooperation at the national and international level, and the strengthening of ethics and valuation of the National Research Ethics Committee (Conep), and the Research Ethics Committees (RECs).

Investments in Research and Development

The legacy of Joseph Schumpeter[23] is a primary reference for addressing relationships that involve innovation and economic development. According to the author, economic growth is a dynamic process and is, above all, a "process of creative destruction", essentially depending on the generation and use of innovations associated with the processes involved in their dissemi-

nation, such as exploring new markets and new business dynamics[5,23,24].

In short, one gleans from this that RD&I/H creates opportunities for investment, employment and income, thus creating an active space of economic development, which according to Viana et al.[25], emerges from adaptations across sub-systems at different moments in time, strengthened by a specific link to the manufacture of medical inputs, equipment, materials and drugs, that today is the main dimension used to define the direction of healthcare policies all over the world.

Historically, the government has been the main source of funding for R&D in Brazil[16,24,26]. In developed nations however, private investment in this area grows faster than government investments, which range from about 2 to 4% of the GDP, as shown in Graph 1. Brazilian government investment has remained pretty much stable since 2008, while private sector investment increased somewhat[27]. Regarding private investment, among BRIC nations Brazil is behind China, which gets more of this type of incentive.

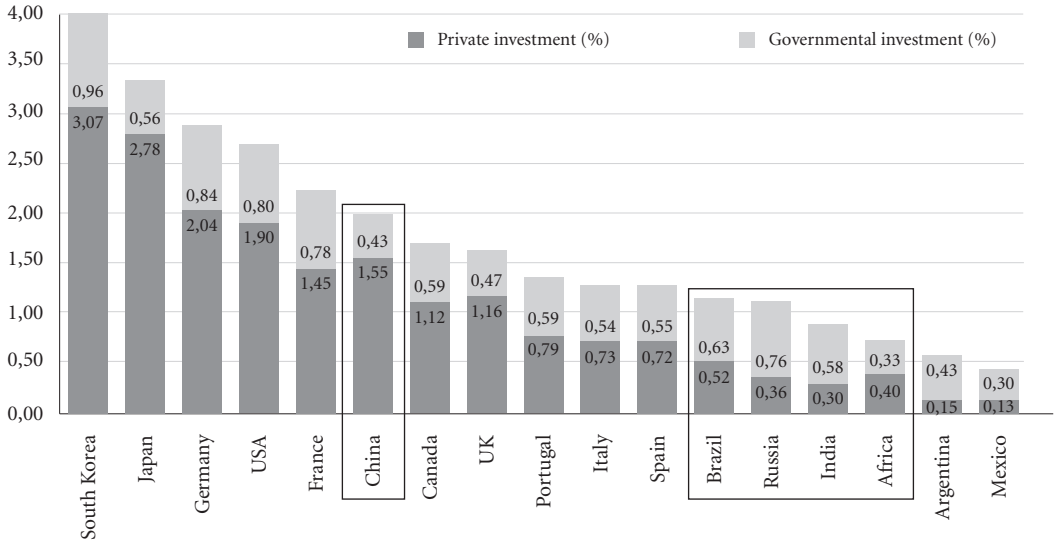
According to the Unesco Science Report entitled *Towards 2030*:

With its strong demand for commodities to feed a fast-growing population, China has protected exporting nations from falling demand in North America and the EU, since 2008. However, the most recent analysis reveals that the commodity boom has reached an end, revealing structural deficiencies, in particular in Brazil and the Russian Federation[27].

Expenses with drugs and the like are quite significant in Brazil. Table 1 compares total spending with drugs and Ministry of Health R&D investment in Pharmaceutical Care compared to the percent total MoH budget over the course of five years.

Promoting ST&I in drugs, medicines and healthcare inputs is believed to be aligned with policies and instruments created to strengthen the area. This premise is supported by Vargas et al.[28], when they talk about the involvement of different players on behalf of a recovery of the Brazilian production base:

[...] *it involves increasing articulation between manufacturing, technology policies and the healthcare area, as well as a return of growth policies, reflecting in the recognition of a strong interface between healthcare and the new biotechnology, nano-*



Graph 1. Government and private investment in R&D as a percent of GDP in different countries.

Source: Ministry of Science, Technology and Innovatoin (2015), Apud Unesco (2015), suitably adapted.

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technology and advanced specialty chemicals-related technological platforms, and their importance to the nation's manufacturing basis [...].

In this sense, one of the strategic areas to foster innovation resulting in new drugs for the population is Clinical Research, which acts as a bridge between biotechnology research and manufacturing. This converges with the debate that includes S&T production for generating inputs to face health issues. In other words, an interface between production & innovation and care is created. The State, as the intermediary, formulates and enforces measures to generate development for the social apparatus[29].

Unlike other market goods such as electronics or food, health is a public asset, also subject to market failures, but one that involves human life, the greatest asset of all[30].

This premise justifies the State's commitment to not give up its regulator role, providing control and vigilance mechanisms that can ensure the safety of healthcare products (drugs, medicines and other inputs), even if the State itself promotes their manufacture[30]. Supporting the healthcare process requires involving numerous different players in a range of networks, built specifically for this context, but without ignoring individual safety and care.

Contributing to this context, Vianna et al.[30] said:

Over time, both productive and social motivations for healthcare were built on discussions involving RD&I on the one hand, and ethics, and the right to and ensured access to quality healthcare services on the other. Over time, understanding how these interests are interrelated was decisive for designing policies and integration mechanisms.

Specificities of clinical research

The priorities of clinical research should be included in all 24 sub-agendas of the National Agenda of Healthcare Research Priorities as a strategy.

Niches with a high potential for success are vaccine and immunobiological production, and new diagnostic techniques. New products for treatment, prevention and health promotion such as herbal medicines, drugs and medicines, blood derivatives, homeopathic drugs and inputs for supplemental practices, as well as health prevention and promotion[11,28].

Even though National Agenda of Healthcare Research Priorities is unquestionably relevant for equal distribution of research funds, it is also essential to consider that, while desirable, professionals are not always ready to use the results. Bringing together those who do research and those who make policies could be a strategy to consider[31,32].

Clinical research as performed at universities and teaching and research institutions contributes to this premise, as it provides opportunities for training healthcare professionals, technical and scientific exchange, development and improvement of teaching and research methods, and new therapeutic options for patients, which can be used by hospital managers to help steer teaching, research and care activities.

According to the National Institutes of Health (NIH)[33]:

Clinical Research is research on human beings (or on materials of human origin such as tissues, specimens or cognitive phenomena), where an investigator (or team member) interacts directly with participants. In-vitro studies using human tissue not associated with a living individual are excluded. Clinical research includes: (a) the mechanisms of human disease; (b) therapeutic interventions; (c) clinical trials; (d) the development of new technologies.

Clinical research is also used by healthcare managers to make decisions, with studies to supplement scientific evidence and subsidize decisions common to the practice of Healthcare Technology Assessment. This practice is based on the premise of defining clinical guidelines and protocols, regulating drug prices and formal policies for assessment, incorporation and management of technologies within SUS[34].

Clinical trials are one type of clinical research, designed to investigate the efficacy and safety of medicinal products and medical procedures in human beings, making it possible for them to be used in medical practice. For the most part they are multi-center, multi-institutional and sometimes multi-sector or multi-national, depending on the complexity involved in the processes in question.

They tend to involve centers of excellence with highly trained professionals using research protocols designed according to strict ethical and good clinical practice criteria, solid knowledge bases and backed by prior studies and knowledge of how the target disease evolves.

The entire clinical process, from planning through study end, must follow well established regulations set by the agencies created to protect participant rights (Conep and Anvisa in Brazil), ensuring results of high scientific quality[35,36].

Table 1. Ministry of Health budget and spending on drugs over time.

Actions	2011	2012	2013	2014	2015
Strategic medicines	162.000.000	124.000.000	134.834.524	164.730.448	340.000.000
Basic medicines	1.060.000.000	1.077.448.725	1.213.500.000	1.292.642.028	1.230.000.000
Exceptional medicines	3.521.496.999	4.082.150.000	4.977.534.000	4.890.845.854	5.867.474.795
AIDS Medicines	804.802.000	823.600.000	770.200.000	864.187.200	1.101.000.000
Immuno-biologicals	1.613.204.809	1.676.500.000	2.181.900.000	2.296.719.000	3.300.672.000
Coagulopathy medicines	412.565.000	552.300.000	747.915.000	583.432.574	802.500.000
Budget drugstores	774.605.000	1.410.000.000	1.856.600.000	2.460.838.514	3.261.328.000
SUB-TOTAL – MEDICINES	**8.348.673.808**	**9.745.998.725**	**11.882.483.524**	**12.553.395.618**	**15.902.974.795**
Innovation and Production	56.860.300	64.900.000	72.720.000	55.525.381	50.160.000
Modernization of the Manufacturing Park	0	130.000.000	160.000.000	106.400.000	46.800.000
Laboratories Official	0	70.000.000	0	0	0
Research	77.337.653	81.392.000	93.685.000	90.305.000	84.128.000
Structing – A.F.	10.972.576	25.000.000	39.000.000	69.399.580	84.152.000
GRAND TOTAL	**8.493.844.337**	**10.117.290.725**	**12.247.888.524**	**12.875.025.579**	**265.240.000**
MoH Budget	63.113.634.859	78.361.160.095	84.051.839.071	108.393.354.888	121.154.205.789
%	**13%**	**12%**	**14%**	**12%**	**13%**

Source: Department of Science, Technology and Strategic Inputs/MoH.

These studies are conducted in phases, as shown in Figure 2. If the results of a phase are positive, the study moves on to the next one.

Each phase in clinical trials must complete certain elements in order to achieve scientifically robust and reliable results. This is general data as, in the case of clinical trials for some pathologies, such as in the complex case of cancer, certain specificities must be taken into consideration.

It is estimated that market introduction of a new drug/medicine requires some ten years of R&D and ~US$ 1 billion in research. This leads to multi-sector agreements involving the government, development agencies, universities, hospitals, etc. for creating public-private partnerships (PPPs)[30].

Final Considerations

The discussion presented herein includes numerous theoretical milestones created over the years, all of which contribute to understanding and listing the elements that have been strengthened in S&I/H and RD&I/H, and how one can take advantage of the windows of opportunity that open up, given the direction inherent to each one.

Regarding the milestones we analyzed, the federal government has clearly made an effort to provide the instruments required to promote the production of health and healthcare. One interesting question is the possibility of a conflict of interest between private enterprise and public healthcare (market vs. State).

It is essential to understand what science, technology and innovation mean within the dynamics of the different players. For example, including the pharmaceutical industry in partnerships for performing clinical trials, using the infrastructure created within the RNPC, may be a strategy to strengthen the necessary development of clinical research in Brazil.

In this scientific scenario surrounding clinical research, the key player is the investigator-entrepreneur, who mobilizes members of the scientific community to identify shared expertise to create a network of collaboration, partnering with the government and private sector to create a "shared management structure".

This teaches us that collaboration as a network, as described by Martins[38], enables the incorporation and sharing of knowledge in production processes. Added to this is the fact that, when signing a partnership agreement and sharing resources, each player enables strategic directionality, in the sense of composing the mission, goals and functions of this type of bond, expressed in the agenda of priorities defined by SUS.

The Healthcare Production Complex undeniably and increasingly needs science to maintain

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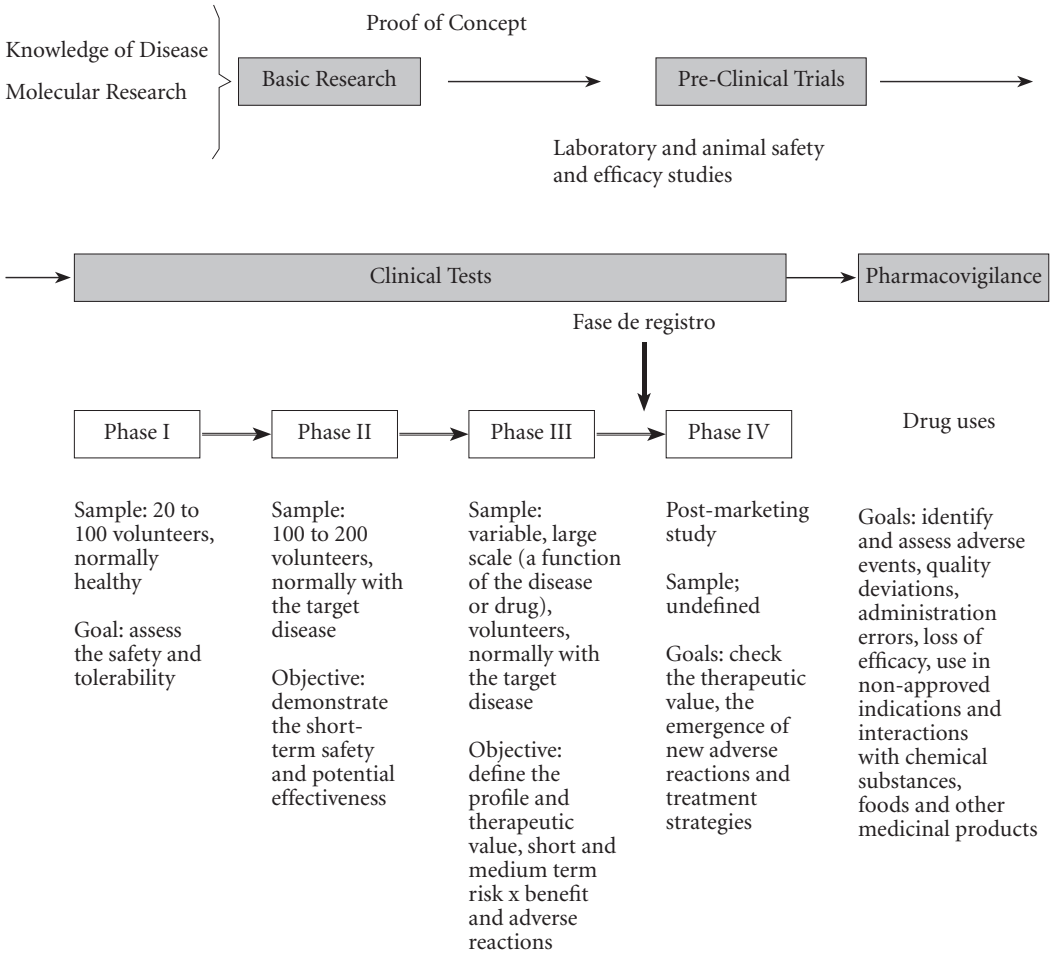

Figure 2. Phases of the Research and Development Process.

Source: Pinho et al.[37].

itself. Clinical research creates scientific knowledge to tackle public health issues, using subsidies to generate new technologies or improve existing techniques, processes and technologies, produced, marketed and sold in the different segments, and thus feeding the entire Economic-Industrial Healthcare Complex.

This movement culminates in the understanding of Dal Poz[39] and the support of Latour's Actor-Network Theory[40], which in addressing the limits of a network, warns us not to limit them to the number of players, but use the environment defined by the flow of artifacts that circulate and enable sharing resources, including financial resources. This environment is nothing more than the National Innovation System, with its set of S&T policies and technology and regulatory regimes. This idea covers networks and their connections.

Thus, assessing these relationships in the context of this article means considering the progressive strengthening and extension of the interaction between the research and development system and the healthcare production system, and its ability to fund itself, and management of the State regulatory structure.

Collaborations

M Tenório helped design and outline the study, gathered and analyzed data, selected the references, drafted the initial version of the manuscript, and revised and approved the final version. GA Mello and ALD Viana helped design the study and participated in the methodological outline of the study. They also helped select literature references, reviewed the initial version and approved the final version.

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