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CLINICAL TRIAL REGULATION: PROCESSUALITY AND PERFORMATIVITY

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Advisor: Prof. Dr. Walter Bataglia
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I dedicate this thesis to my beloved wife
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ABSTRACT

This thesis aims to understand, under a procedural and performative approach, how regulation is constructed and developed. I adopted a procedural, relational and sociomaterial ontological perspective, using the actor-network theory, in its seminal version, developed by Bruno Latour, Michel Callon and John Law, to describe the activity raised by human and non-human actants (objects, quasi-objects and hybrid artifacts) generators of controversies that, in networks, relationally, promote the fluid character of reality. This procedural activity also has its moments of reifications, stabilizations or provisional punctuations, in addition to generating displacements called translations that give a dynamic character to realities through the closure of controversies, which in the actor-network theory we call black box closures. The research takes place through the monitoring of a process of reconstruction of the regulatory apparatus affecting the business segment of Brazilian clinical research, arising from the productive chain of research and development in the pharmaceutical sector, taken as a whole as a meta-organizational reality. The study encompasses activities that took place during the current legislative process in the Brazilian legislative power, which seeks to establish a legal framework for clinical research, in which a new regulatory system would be erected to replace the current regulatory model. ANT, which is known for revisiting the modern and substantive concept of groups, organizations and society itself, is also adopted here for the reconstruction of the very notion of regulation, of a stabilizing and controlling bias, but which is presented in the thesis as an artifact relational and procedural socio-technical, whose dynamics is explained by its performative character. The performativity of regulation is verified bidirectionally, in the infra-relational aspect, involving the associations of actants that participate in its reassembly, in the activities of the legislative process observed during the work carried out under the Bill of the Brazilian Federal Senate (PLS 200/2015, converted into the Bill of the Chamber of Deputies, PL 7082/2017) as well as in the normative revisions that took place within the scope of the National Health Council (CNS) that instituted and maintains the CEP-CONEP system that regulates the current ethical instance of Brazilian clinical research. Performativity is also observed in the inter-relational aspect, from the interactions that the regulatory artifact maintains with other elements that integrate the relationships of other macro-actors in the network, such as research sponsors, the scientific community, research participants and patients, and their representative groups. The methodological path followed an abductive approach using the technique of cartography of controversies. As a result of the work, it is possible to understand that regulation, unlike understandings focused on the centrality of human will and a substantive ontology, when studied in procedural and performative terms, is better recognized as a relational aggregate of heterogeneous elements rhizomatically fragmented that dislocate spatiotemporally by actors-networks.

RESUMO

Esta tese tem por objetivo entender, sob uma abordagem processual e performativa, como se constrói e desenvolve a regulação. Adotei uma perspectiva ontológica processual, relacional e sociomaterial, valendo-me da teoria ator-rede, em sua versão seminal, desenvolvida por Bruno Latour, Michel Callon e John Law, para descrever a atividade suscitada por actantes humanos e não-humanos (objetos, quase-objetos e artefatos híbridos) geradores de controvérsias que, em redes, relacionalmente, promovem o caráter fluído da realidade. Essa atividade processual também possui seus momentos de reificações, estabilizações ou pontualizações provisórias além de gerarem deslocamentos denominados de traduções ou translações que conferem o caráter dinãmico às realidades por meio de encerramentos das controvérsias, o que na teoria ator-rede denominamos de fechamentos de caixas-pretas. A pesquisa ocorre por meio do acompanhamento de um processo de reconstrução do aparato regulatório incidente sobre o segmento empresarial da pesquisa clínica brasileira, oriunda da cadeia produtiva da pesquisa e desenvolvimento do setor farmacèutico, tomado em seu conjunto como uma realidade meta-organizacional. Foram estudadas as atividades ocorridas durante o processo legislativo em curso no poder legislativo brasileiro e que busca estabelecer uma marco legal para a pesquisa clínica, no qual um novo sistema regulatório seria erigido em substituição ao modelo regulatório em vigor. A ANT, que é conhecida pela revisitação do conceito moderno e substantivo de grupos, organizações e da própria sociedade, é aqui também adotada para a reconstrução da própria noção de regulação, de viés estabilizante e controlador, mas que é apresentada na tese como um artefato socio-técnico relacional e processual, cuja dinâmica é explicada pelo seu caráter perfomativo. A performatividade da regulação se verifica bidirecionalmente, no aspecto infra-relacional, envolvendo as associações de actantes que participam da sua remontagem, nas atividades do processo legislativo observado durante os trabalhos ocorridos sob o Projeto de Lei do Senado Federal Brasileiro (PLS 200/2015, convertido em Projeto de Lei da Cãmara dos Deputados, PL 7082/2017) como também nas revisões normativas ocorridas no âmbito do Conselho Nacional de Saúde (CNS) que instituiu e mantém o sistema CEP-CONEP que regula a atual instãncia ética da pesquisa clínica brasileira. A performatividade também é observada no aspecto inter-relacional, a partir das interações que o artefato regulatório mantém com demais elementos que integram as relações de outros macro-atores da rede, como patrocinadores de pesquisa, comunidade científica, participantes da pesquisa e pacientes, e seus grupos representantivos. O percurso metodologico seguiu uma abordagem abdutiva com emprego da técnica de cartografia de controvérsias. Como resultado do trabalho é possível compreender que a regulação, diferentemente das compreensões voltadas para a centralidade da vontade humana e para uma ontologia substantiva, quando estudada em termos processuais e performativos, é melhor reconhecida como um agregado relacional de elementos heterogêneos fragmentados rizomaticamente que se deslocam espaço-temporalmente por atores-redes.

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LIST OF ABBREVIATIONS

ABRACRO - Brazilian Association of Representative Organizations of Clinical Research
ANA - National Agency of Water
ANAC - National Agency of Civil Aviation
ANATEL - National Agency of Telecommunications
ANCINE - National Agency of Cinema
ANEEL - Agency of Electric Power Agency
ANP - National Agency of Oil, Gas and Biofuels
ANT – Actor-network theory
ANTAQ - National Agency of Waterway Transportation
ANTT - National Agency of Land Transportation
ANVISA – National Health Surveillance Agency
CACON - Center for High Complexity in Oncology
CAS - Social Affairs Committee
CCJ - Constitution and Justice Commission
CCT - Science and Technology Committee
CEP – Research Ethics Committees
CIOMS - Council for International Organizationsof Medical Sciences
CISCRP - Center for Information and Study on Clinical Research Participation
CMED - Resolution of the Medicines Market Regulation Chamber
CMO – Contract Manufacturin Organization
CNP - National Petroleum Council
CNS – National Health Council
CONEP – National Committee on Research Ethics
CRO - Contract Research Organization
CSS - Social Security Commission
DNC - National Coffee Department
ENCEP - National Meeting of Research Ethics Committees
FOCEP - Permanent Forum of Ethics Councils in Research
GCP - Good Clinical Practice
HCI - Hospital de Caridade de Ijuí
IAA - Institute of Sugar and Alcohol
IBC - National Institute of Coffee
IN - Normative Instruction
INC - Joint Normative Instruction
INM - National Institute of *Mate* Tea
INP - National Institute of Pine
INS - National Institute of Salt
INTERFARMA - Pharmaceutical Research Industry Association
IRB - Reinsurance Institute of Brazil
MRCT - Multi-Regional Clinical Trials
PAHO - Pan American Health Organization

PHRMA - Pharmaceutical Research and Manufacturers of America
PL – Draft Bill of Law
PLS – Draft Senate Bill
PRT - Ordinance
PRTC- Joint Normative Ordinance
R&D - Research and development
RD - Resolution
RDC - Collegiate Board of Directors
RIA - Regulatory Impact Analysis
SBPPC - Brazilian Society of Clinical Research Professionals

Summary

1 MEMORIES

I start this research with a deep reflection in the form of memories in order to share with my examiners and future readers the motivations, interests, justifications and epistemic questions I came across while carrying out the research project.

Since the first contact with academic activities I had an intuitive sense that Science is neither neutral, timeless or universal. When I did my master's thesis, exactly 10 years ago, I mentioned Feyerabend (2003) who said that observation of everyday life facts is more based on opinions than on things. Subjectivity is inexorable in Science, which means that the understanding of the researcher's trajectory helps to understand his or her work.

Almost a decade after my experience in taking the Master's degree, my subjective instinct has expanded, and is now reinforced by the speech of Versiani (2005), who defends a dialogical subjectivity explained in autobiographical narratives as a way of recognizing motivations, anxieties and choices of the journey that permeate the researcher's investigative activity.

From this research, I would highlight in this subjective experience the mediation of things and objects as part of the interactions that trigger findings and elaborations that now recognize non-human agency as a way to understand reality.

The work that I propose to carry out here does not have an autobiographical intention, but I could not fail to make use of my life story and of the controversies that generated some of the choices made, including the reason to accomplish this thesis. Therefore, I am going to tell my life story with socio-material and performative characteristics, now incorporated to the new approach I learned.

My father worked in a factory, was catholic and had a pragmatic personality, while my mother was a protestant teacher with Parnassian characteristics. I am the oldest of five siblings, who were expected to follow their father's steps. According to his point of view, I should work at one of the automobile companies in the industrial region of the state of São Paulo, known as ABC (named after the cities of Santo André, São Bernardo as São Caetano). However, my mother's influence prevailed, and before starting to look for a job I finished my studies. I would have a very quiet social life, filled with classical music at the Protestant church, and was certified as a classical guitarist.

At the same time, I was often asked to get involved in the routine of a small sawmill that my father kept at the back of our house. Besides being a hobby, it helped to increase the family's income.

I grew up in an ambiguous, conflicting and heterogeneous environment, in which material and subjective, sacred and profane, popular and erudite culture, working people and middle-class ones existed at the same time. I imagined that I had to make choices, but little by little I realized that none of these influences would be followed.

As a child, my favorite subject was mathematics, but by the time I was 10 years old I read the political sections of the newspaper "O Estado de São Paulo" every day. When I was a teenager I started to consider the possibility of taking a bachelor's degree in Political or Social Science, although my father used to say: "you won't make enough money with that, son!".

I attended a technical public school, once again living an ambiguous experience, since neither did I attend a classical or humanist course – as this was not affordable – nor did I take an industrial apprenticeship course with emphasis in mechanics, as this was not what I wanted. Then I found an alternative and took a data processing course, although I did not know exactly what that meant. I learned the computer languages and the logic of information systems, but this was a short experience.

When I had to choose a superior education course, this ambiguity was at its highest, and therefore I chose a course that would satisfy my personal desire and that I believed would somehow meet my father's expectations: I decided to study Law. This choice proved to be wrong then right, respectively.

My parents were really upset, as they associated the profession with dishonesty, and thought that I would be introduced to crime, deals and crisis. Unconsciously they wanted to protect me from the controversy present in the daily life of an attorney. However, as I was of age, they no longer had much control over my decisions and – although extremely suspicious – decided to support me. This encouraged me to search for excellence, since I was committed to prove that I had made the right choice.

In 1991, I was admitted to the Law School at Universidade Presbiteriana Mackenzie and chose a challenging, but promising area. I decided to have a public service career and become a judge. The internships at the State Attorney's Office, at the Public Ministry of Labor and at the School of Magistracy of the São Paulo Court of Justice were part of my project, and I had a good performance in these experiences.

After completing my bachelor's degree, I signed up for public examinations and managed to get some approvals in the early stages of the exams. However, life reminded me that my career would be more diverse. My father had become an entrepreneur and, after the first business failure, he opened a new business – a small metallurgical company. He thought he

should help me in my early career, and that I should help him in return, although I was a young lawyer attempting a public service career, and he was a person starting a business.

Since I had no experience or enough money, I ended up by giving up my dream of being a judge, and instead I had to perform all kinds of tasks in that family business.

I did my best to understand how adversity could become opportunity. I chose to study Business Administration and my father and I became partners in order to make the family business grow. The plan was to prepare the company to be sold, and I would then keep the profit of the sale to invest in my career as an Attorney.

This time the plan turned out to be right, then wrong, respectively. The company thrived and was successfully sold after a few years. However, this experience proved that diversity was the best way for me. I had never stopped working as a lawyer, but in search of making the family business grow I attended Business School, and became a Master in Business Administration, one of the areas of knowledge that perhaps best shows my eclectic profile. As I had embraced my mother's faith, at the age of 24, I was teaching Bible Sunday School, where I realized that I enjoyed teaching.

At this point I want to make a reflection to summarize everything that I had done so far. I was a young protestant, a locksmith's assistant, a classical guitar player, a system programmer, a theology student, a lawyer, almost a judge, an entrepreneur, a manager of a small company, a Master in Business Administration who was now decided to be a teacher. What should I teach? It was a difficult decision, as I had had so many experiences, but at the same time I did not have deep knowledge in any of them.

I was hired by Universidade Presbiteriana Mackenzie shortly after I had completed my Master's Degree, and my proposal was to teach anything related to business strategy, people management, business law or entrepreneurship. This eclectic ability is not so common at universities, but I then realized that while teaching I was able to enrich the classes through all this previous experiences, since my knowledge in several areas enabled me to transcend the contents of the books approached in the formal disciplines. I accomplished experience because it was part of my job to deal with clients, employees, suppliers, banks, partners, technological obsolescence, cash flow and several laws and regulations that consumed our profits.

Years later I was recommended by a friend to teach Law at a school in the ABC region. Once again I accepted the challenge to be eclectic, and started teaching civil law, procedural law, labor law, business law, constitutional law and administrative law, besides introductory disciplines. It was a great effort to master so many disciplines, but it was pleasant to teach in this multidisciplinary way, instead of being limited to a single area of knowledge.

I believed in the integrated view of facts and subjects in order to achieve a better understanding, and I wanted to share this with my students. This combination of different knowledge brought the “hybridism” and “association” to the building of my career and my own identity, in the midst of conflicts or controversies. It was just then that I decided to take one more challenge, and achieve the title of Doctor in Business Administration.

Initially, I chose the contractual area to start my research, as this is a legal and economic subject, with different models, and ranges from interpersonal relations of marriage to the vertical limits of the theory of the firm, and even reaches the relational stigma that has been integrating the Psychology & Law studies.

Unconsciously, I was again searching the multidisciplinary aspect of things. However, there was a contradiction, since I insisted in making plans despite the experiences I had already gone through. It was as if I hadn't understood the social dynamics that is present in life and had once appeared in the past.

In the new school semester of 2016 I was invited to teach administrative law to undergraduate law students, and so I had to deepen my knowledge about legal theory of the administrative act. I came across the several possibilities of interaction between public administration and private individuals, ranging from the mere permission for a newsboy to set up a newsstand to complex public-private partnerships for the construction of ports, airports and practically all infrastructure projects that are known in Brazil.

In 2017 I participated in a Congress at the Faculty of Law of the University of Lisbon, and there I attended interesting discussions about the gap still open about issues regarding “what”, “when”, “how”, “who” and “why” to regulate. Lawyers, economists, public and private administrators reported their experiences in a unified tone of complaint about the so-called “regulation failures”, in an analogy to what we know as “market failures” in economic sciences.

There are sectors in which there is a regulatory deficit and countless others for which regulation would constitute a real overwhelm, but with no clearness regarding conditions, parameters or objects the regulation should focus on. Therefore, there is a demand for the creation of a “general theory of regulation” that is necessary to qualify the countless decision-making processes of public-private (meta)organizational interactions.

Right at the beginning of the PhD program, new demands were presented to me. In a conversation with my advisor, Professor Dr. Walter Bataglia, I accepted to participate in his research group that was already underway, which would imply that my thesis would be developed in the pharmaceutical R&D (research and development) sector. I went through many

experiences, but nothing that brought me back to this sector. However, I faced the new challenge as a natural process, since I was used to dealing with different subjects..

From a theoretical point of view, the first discussions approached the New Institutional Economics, whose framework was suitable for the purposes of addressing the outsourcing processes of clinical research activities, which gave rise to the segments of the so-called CROs (Contract Research Organizations) of the pharmaceutical sector.

It turns out that the concern was about understanding the process of change that gave rise to the CROs and, afterwards about how the regulatory environment was changing, bringing significant reflections regarding the competitive position of this segment in Brazil. During the PhD program I was introduced to Professor Harry Sminia, from Strathclyde Business School, Glasgow, Scotland, an expert in process approaches. I realized that my subject was no longer the contract, and that a deeper understanding of the regulatory dynamics of a complex sector that was riddled with conflicting interests would require new approaches.

Under the influence of Professor Walter Bataglia, reinforced by the co-supervision of Professor Harry Sminia, I gradually got to know the different approaches to processes and their onto-epistemological implications.

I entered the doctoral program with this latent restlessness and, although the first attempts at drafting a project were directed towards contractual structures arising from economic neo-institutionalism, the conversations we had about the competitiveness of the clinical research sector soon led me to the regulatory problem.

My paper came to be the very moment I joined the research group led by my advisor Professor Walter Bataglia, who has been studying competitiveness in the pharmaceutical sector for over a decade. From that moment on, my alleged theorizing on regulation found a favorable locus for work: the clinical research segment of the pharmaceutical industry.

First the interest was centered on the institutionalization of interactions between the 'economic sector' and the 'market'. I wanted to understand the various conflicts of interest that permeated pharmaceutical R&D when it came to pricing its products, driven by the logic of profitability, opposed to the interests of customers who claimed the right to health treatments. I also noticed the problem of delays in the release of medication under development, and how such conflicts were mediated by the State through the action of ANVISA, responsible for such releases, and by the Public Health System (SUS), which offers free medication to the population.

All this led me to the issue of judicialization, which involved important demands on requests for authorization of the use of experimental medication and to the condemnation of the

State to pay for medicines approved by ANVISA, but not yet incorporated by SUS. The repercussion of the phosphoethanolamine pill, intended for the treatment of different types of cancer, as well as the situations of ultra-rare diseases, as in the case of the release of Spinraza for the treatment of supraspinal paralysis, were emblematic to understand the topic.

I then came across a very interesting article written by Cerretto and Domenico (2016), according to whom change can be understood according to a substantive view, whose process leads an entity from one state to another, without changing its essence, which translates into a punctual or episodic phenomenon. However, in an ontologically procedural approach, reality is explained by the continuous flow of relations that precede institutions.

As the empirical studies conducted under process-based ontologies would be underrepresented in organizational studies (LANGLEY; TSOUKAS, 2016), the next step was to realize the existence of research opportunities under the Actor-Network Theory (ANT) approach, developed by Bruno Latour, Michel Callon and John Law, which is based on a flow ontology, but with very peculiar assumptions and postulates.

I was interested in the ideas of authors of ANT for three reasons: (a) the innovative view about the concept of social and heterogeneous aspects of life perspective resulting from it; (b) the approach to a new interaction between objectivity and subjectivity; and (c) the idea of translation as an explanatory process for the constitution of reality from the notion of controversies.

First of all, when Latour (1994) says that we are hybrids, belonging to scientific institutions, somewhat engineers, somewhat philosophers, transported by wires or networks, amidst confusing stories, I felt this was about my own story, whose constitution and trajectory took place through a process of “translation”, “mediation” and “purification” of elements hitherto which I also used to consider dissociated. So I understand that other people’s judgment, not I was the problem.

Second, the possibility of association between humans and non-humans sounded like music to my ears (LATOUR, 1994; CALLON, 1986). Something that sounds strange to a modern sociologist shouldn't have the same effect to an attorney. All the time legal professionals deal with processes of personification and de-personification of facts and objects. We transform objects into people and vice versa, and we do it with no constraints.

The subject-object dyad is marked by the attribution (or not) of rights and obligations to entities. If a set of assets is given the ability to securitize rights and obligations those assets become people; if this attribution is removed, it becomes an object. A partnership contract or a legal act becomes a person in the form of a partnership; a heritage complex is personified in

foundation. An unborn child's personality is conditioned to a future and uncertain event, while an animal is a moving thing, although it manifests its will. Everything, after all, is convention, but with the force of agency to generate interactions and feed the flow of change.

Likewise, the "almost objects", such as laws and contracts, and a countless list of hybrids, are the result of manifestations of collective wills that detach themselves from their makers to assume their own voices and raise relevant controversies, even against interests of those who caused them. And the list goes on. What can we say about living microorganisms that are capable of changing the course of human history, like what we have just witnessed? The acting power of these non-humans, either alive, objects or quasi-objects cannot be denied.

Third, the notion of translation, which represents the core of ANT's approach, translates exactly the transformation processes of the realities that are being produced through the controversies, confrontation or conflicts positions of underlying interests to people's opinions, things, hybrids and their associations.

I would say that the actor-network theory may present itself as one of the promising approaches to understand dynamic, complex and constantly evolving realities like the one we intend to unveil in the processes involving the clinical research segment inserted in the pharmaceutical R&D (Research and Development) activities.

In this approach I foresaw the possibility defended by ANT of understanding, in a flow ontology, the process of change through interactions qualified by controversies (LATOUR, 2007), very present and intensified by the clashes waged by institutional actors in which they joined around the interests represented by patients, participants in clinical research, the scientific community, research sponsors and regulatory authorities in the Brazilian segment of clinical research. However, ANT may also lead us to recognize that eventually even other actants (terminology adopted by ANT to designate actors), represented by microorganisms, genetics, biotechnology, laws, contracts and court decisions are also protagonists of this dynamics.

Such recognition may make us sensitive to the perception of resignations about the very concept of health, disease, pharmacological intervention, the economic sector and the state regulation involved, which would even affect the understanding of clinical research as we know it nowadays.

This path has already been taken by Latour (1993) in his pursuits on the agency of microorganisms in the development of food pasteurization process, and this leads us to think that the true dynamics to be faced will depend on the recognition of the association of hybrids, by which it is accepted that the standard, the bacteria, the patients' DNA, court decisions and

the genetic sequencing software have relevant influence for the analytical understanding of a reality that is only possible to see in flux.

However, reflections throughout the research also produced concerns, which enabled the building of this thesis. The big issue to be faced is whether the notion of translation, presented by ANT and raised by controversies amidst the association of human and non-human actants is sufficiently understood, and if it can be managed from the use of a performing mentality built from John Austin, who has no tradition in ANT, but who has proved to be totally in accordance with this approach, especially from Michel Callon's (1998, 2007) work.

The project was then to understand a "becoming". An effort was underway to change the regulatory status through the strategy of creating a law to establish a regulatory framework for clinical research, and thus decrease of power of regulatory agencies and bodies. Therefore, an approach focused on what is happening and not in pre-existing reality would be necessary.

Now I invite the reader to see the introduction, in which the problems, objectives and postulates of the research will be duly presented and justified. I want to reinforce the intention of highlighting the backstage of this work, which was developed and gradually gained socio-material and performative characteristics. This narrative concerning my experience attests that I have been eclectic throughout my life.

So far I have just organized some ideas that enabled me to explain what the purpose of this paper is.

2 INTRODUCTION

This thesis proposes the establishment of a new concept for regulation, from the procedural and performative lens, making use of the approach found in the actor-network theory.

But to make our proposal clear, in this introduction I will look back at the relevance and importance of the topic, focusing on the fact that the regulation to be studied involves the clinical research activity of the pharmaceutical R&D sector, in addition to indicating the onto-epistemological assumptions adopted. at work.

In the field of organizational theory development there is a growing interest in understanding the environment, which is characterized by the set of phenomena external to organizations with the ability to influence them (HALL, 2004).

Such factors are not just limited to operational interactions, which are established based on resources, information, markets and competition, but also involve a set of institutional factors, translated by cognitive, normative and regulatory elements that also interfere with the identity and even livelihood of organizations (SELZNICK, 1955; SCOTT, 2008).

Concerning specifically regulatory aspects represented by the institutional understanding of the influence of current laws and rules regarding dynamics of the organizational process (SCOTT, 1995), a framework was developed in which the very activity of regulating is manifested the epithet of “regulatory organizations or agencies”, known as a result of the phenomenon of “agencified regulation” (GUERRA, 2015).

Regulatory agencies would be an expression of the personification of regulatory institutions of public-state nature, with great influence on people and private organizations subject to them, without ignoring that the regulated subjects also influence and shape the agencified regulation.

The complexity of these interfaces between organizations and environment, more specifically regarding regulatory aspects, offers an opportunity for such phenomena to be observed under approaches that favor a procedural view, more dynamic and consistent with the search for how these phenomena are constituted (LANGLEY, 1999; TSOUKAS, 2010).

In these interactions, private organizations and the economic segments to which they are inserted, together with regulatory bodies linked to economic sectors acting in a symbiotic relationship, wage real battles whose effects enact or constitute an identity that we would call 'meta-organizational' (AHRNE, 2005; KAUFFMAN, 2017).

This new ontological and procedural-relational lens brings with it the concern about how these meta-organizational realities are constituted and sustained, represented by complexes of relations that involve people, organizations and the State under the various forms of direct, indirect or agencified action.

However, if the ontology of a process in flux values becoming, continuity and impermanence, how can one explain the creation and maintenance of supposedly stable or long-lasting institutions? And, even if repeated movements of provisional stabilization are accepted, what is the driving force of this process?

These issues deal with the metaphysical dimension that seeks to understand the nature, origin, composition and how the elements that give existence to social phenomena perceived as institutions of reality are related.

A possible answer can be postulated by taking as reference one of the contesting strands of classical or traditional sociology, called Actor-Network Theory, also known as the acrostic "ANT", led by Bruno Latour, Michel Callon and John Law, researchers at the Center for Sociology of Innovation in Paris and sponsors of the French School of Science & Technology Studies (STS).

Michel Callon and Bruno Latour (1981) tackled these issues offering new perspectives for the relations between macro and micro, agency and structure, and actor and system. They did not make use of dialectical equations or circular explanations between the whole and its parts, but conceived a new movement based on a number of associations created by connected micro-actors that promote displacements or translations.

They wanted to understand how a multitude of people get to the point of acting as if they were an individuality, as it occurs regarding a multinational organization or even with the State itself (LATOUR, 1996).

According to them, what we understand by macro or micro actors is in fact the representation of the same people in different states (as water in its liquid and solid state), being impossible to explain the collectivization process, except through a movement originated by heterogeneous monads that open a path paved by mediators, generators of transformations when associated to form networks (CALLON; LATOUR, 1981).

These authors then argue that a macro order consists of the success of actors in translating the will of other actors into an individual will through which they would start to speak.

This perception of collectivization, of a relational and procedural nature, requires a new understanding of what is commonly understood as "social". This attribute could not be taken

as an explanatory quality of institutions, as it would be the one, the “social”, the result of a movement that constitutes it relationally (LATOUR, 2007).

However, how can this constitutive process of social phenomena be explained? And how does this enable a new ontological understanding of social reality?

ANT advocates that social reality is triggered by controversies that are activities carried out by actors, also called actants that generate translations, weaving social reality, which becomes ontologically understood as relational, procedural and fluid (LATOUR, 2007).

The controversies in ANT are conflicting phenomena that raise debates, are resistant to complexity reduction and are capable of describing the social in its most dynamic form (VENTURINI, 2010a).

Translations, on the other hand, are understood as a process of minimizing controversies (LAW, 1992), or the combination of several distinct interests in a single composite objective (ALCADIPANI, 2010), and also defined as a negotiation process (CALLON, 1986) or displacement (LATOUR, 2007).

ANT does not focus on established a priori figures such as what is currently understood as institution, organization, family or the State. Actants do not pre-exist associations and collective entities are mere reified patterns of provisionally stable networks, whose nature consists of an entanglement of relationships moved by controversies and translations into an ontologically relational reality (LAW, 1992).

ANT also questions the action as interfering with intentionality, voluntariness, causality and attributed exclusively to human agency, and starts to consider the participation of non-humans (objects and quasi-objects) in the relations, in absolute symmetry with humans (CALLON, 1986), in the agency of controversies and translations that constitute the social (LATOUR, 1999).

Therefore, materiality alongside procedurality is a second aspect to be considered in this search for a new understanding of meta-organizational realities.

Regulation, personified by regulatory agencies or State bodies, together with organizations and people affected by it, constituting a meta-organizational complex that is recognized in this thesis as an arrangement of ontologically defined relations due to its procedural and fluid nature, is also explained by such networks in which non-human elements have agency in a status symmetrically equivalent to humans, whose associations explain social reality since they are controversial and transferable,.

It is necessary to advance in the understanding of the process of constitution of reality, which cannot be explained solely by an overt, ready-made or finished approach. Reality is

performative, that is, relations give new meaning to action and reaction mutually considered as a dynamic of reciprocal affectation, in the sense that the elements that constitute the social act at the same time they are led by others to act (NARDACCHIONE; ACEVEDO, 2013).

Performativity, which has great influence and adherence to ANT, has its origins and development in several theoretical traditions, starting with the works of John Austin (2007), focused on linguistics, Judith Butler (1997), in her studies on the self-constitution of actors, and Karen Barad (2003) with her contribution on sociomateriality.

However, it was with the works of the authors of ANT, in particular Michel Callon (1998, 2007), that the performativity thesis gained relevance to the purposes of the thesis, starting from the postulate that natural sciences intertwined with social sciences contribute to the achievement of the realities they describe.

From the development of a performative mentality, it can be conceived, aligned with the actor-network perspective, that the regulation that permeates the strategies of the organizations to which they are attached is seen as a relational socio-technical arrangement that presents itself as an effect of construction of reality at the same time that it acts on the same reality that gave rise to it, through activities that in this thesis we call intra and inter-relational.

In the search to understand performativity in the configuration and reconfiguration of collectives, it is assumed that what gives consistency to regulation is controversy, the natural promulgator of entropy, or tendency to disorder, that is compensated with a counterforce in the sense of aggregating the collective, not dispersing it.

2.1 Why ANT?

From a theoretical point of view, the research course was built in an effort of several attempts at mistakes and successes. Initially, I sought to understand the phenomena mentioned above through deterministic approaches of sociological institutionalism, in addition to considering the study of regulatory dynamics according to an institutional process based on formal and informal institutions. After that, I made a quick foray into Antony Giddens' theory of structuration, in an attempt to understand the institutionalization process in an approach that evaluated the duality of agentic and structural influences on the regulatory process.

However, from the moment I got in touch with the approaches of the process and the promise to understand the regulatory dynamics in a fluid and descriptive way, trying to understand what really happens in the real world, and not by a normative bias or a hypothetical-

deductive mentality, the desire to get closer to non-traditional theories and more longitudinal approaches appeared.

I did a doctoral internship at Strathclyde Business School, in Glasgow, UK, and there I had the opportunity to work with Professor Harry Sminia, interested in alternative approaches to the study of organizational phenomena, notable for his onto-epistemological approaches to processes.

I could understand that ontologically there were different approaches based on processes, especially from the work of Langley and Tsoukas (2016). These authors distinguished the processes of weak perspectives – a set of events or incidents seen chronologically in an entity, considered as supposedly stable – from those of strong perspectives – reality as a "becoming" so that each moment is qualitatively different to the point in that an entity could only be understood through its interactions in constant temporal variations.

As I approached the various process theories, I became interested in the actor-network theory, although I recognized from the outset that it was a theoretical aspect that would challenge me due to its complexity and difficulty in putting it into practice.

I would have to reframe regulation, a phenomenon strongly associated with statics and which would come to be designated by a dynamic and procedurally fluid ontology. It would also be a challenge to consider that the procedural nature of regulation would start to be constructed according to a process that relied on non-human participation.

However, a fluid and material ontology should be considered from specific observations that explain reifications and by performative mentality that focuses on change at the expense of movement.

Therefore, the challenge would be to produce a research in which regulation received a procedural, material and performative look.

Annemarie Mol (2010, p. 261) was right when she made a warning referring to the ANT: "Be careful. No one will hold your hand while you walk."

2.2 Search Field

The work of description of the regulatory artifact, under a procedural-relational, material approach that seeks to identify performativity movements, will encompass business organizations, the scientific community, government entities and natural persons, in addition to non-humans, objects and quasi-objects associated with the networks of actors, all of them appearing as members of a meta-organization inserted in the productive chain of research and

development (R&D) of the pharmaceutical sector that carries out clinical research in the development of medicines, equipment, supplies, components and health services.

It is an appropriate locus for the enterprise, considering the socio-technical nature of the heterogeneous elements that constitute the actors-networks of this system, in addition to the high level of instability caused by the controversies between its participants.

Clinical research is defined as an activity to investigate the effects of administering a new product on a group of human beings and prove its safety and effectiveness, evaluate the recommended dose of the product and verify if there are any side effects before this product is approved for production and sale (GOMES et al, 2012).

The controversies raised in clinical research involve interests that are intertwined by a network of interactions held by key vectors for human existence (INTERFARMA, 2019).

We compared interests of patients in search of health treatment, research participants, sponsors, researchers and research proponent centers, besides regulatory agents inserted in the state control structure of this activity.

Among the organizations that carry out clinical research, the Contract Research Organizations (CROs) stand out. They were created from outsourcing processes of this phase of pharmaceutical R&D, and became responsible for providing pre-clinical tests, analysis laboratory tests, formulation, regulatory advice, clinical trials and post-marketing studies.

The clinical research segment became globally relevant, and is a technological services market with its own characteristics, dynamics and actors, whose revenues are of US$ 112 billion annually, which is equivalent to about 65% of the total global private investment in R&D in the pharmaceutical sector, according to 2019 data obtained by Interfarma - Association of the Pharmaceutical Research Industry.

Clinical research activity is strongly regulated by the State, which pressed by public interest, controls the ethical and sanitary aspects involved in the undertakings of the pharmaceutical R&D sector.

In Brazil, such regulations are made by bodies and legal entities of complex nature, called, respectively, the "National Committee on Research Ethics" (CONEP) in association with the "Research Ethics Committees (CEPs) that together are commonly known as the “CEP-CONEP System”, responsible for the ethics regulation of clinical research. Regulation is also carried out by a regulatory agency called the “National Health Surveillance Agency (ANVISA), which responds for health in the Brazilian clinical research.

The controversies that guide the conflicts of the actors involved in this system, which we qualify as meta-organizational (AHRNE; BRUNSSON, 2005) can be summarized by the search

for efficiency in the process of conducting clinical research, opposed to safeguarding the control of this same process, as guarantee of the rights and protection of research participants.

Brazil suffers from an alleged distortion between its position in the world ranking of the pharmaceutical market (6th place) and an alleged Brazilian under-representation in the clinical research ranking (24th place), with only 2,1% of global studies carried out in 2018, according to the Research Pharmaceutical Industry Association (INTERFARMA, 2020).

On the one hand, Brazil enjoys population demography favorable to clinical trials due to its diverse ethnic composition. Operating costs are comparatively lower than those incurred by the main competitors in Latin America, the United States and Europe. It is also recognized that the level of the agents involved in the system is high: sponsors, regulatory agencies, ethics committees, researchers and a multidisciplinary network of technicians and scientists (GOUY et al, 2018).

However, the following are shown as causes for low participation of Brazil in the world segment of clinical research: (a) long time for research approval; (b) uncertainty regarding the rules of activities of regulatory entities, both in ethical and sanitary spheres (considered subjective and discretionary); (c) insufficiency of resources to carry out regulatory processes more efficiently (INTERFARMA, 2019).

Due to this situation several mobilizations have taken place. The aim is to develop the clinical research segment in Brazil. Among these, stand out the presentation of a Bill of Law before the Brazilian Federal Senate, under number PLS 200/2015, converted into Bill number 7082/2017, pending at the Chamber of Deputies.

Its proponents aim to create a law whose main objective is the reformulation of the CEP-CONEP System through the creation of a regulatory framework for clinical research in Brazil, in order to remove the obstacles that generate slowness in the process and thus bringing positive impact in the competitiveness of the sector.

On the other hand, reaction to the bill has been strong and the actions taken by its antagonists have succeeded in casting doubts on whether this bill really collides with the stated objectives and if it will be approved.

It has been interesting to observe that in this process of rebuilding a meta-organizational system it is possible to glimpse the agency of humans, non-humans and their associations that even without the final result of the legislative activity have raised a performative effect, building a new reality for the segment and for the very regulation, which remains in full activity.

2.3 How my search path occurred

As emphasized by Law (2007) and, considering the wide spectrum of regulation, it was necessary to choose a specific situation to be studied from the perspective of ANT.

On the other hand, an ANT research is not done through clear, defined or pre-conceived steps, being more consistent the use of a rhizomatic perspective, in which it is understood that, instead of a linear, well behaved and with defined characters narrative, reality can be described by anti-narratives that are fragmented, non-linear, incoherent, inappropriate and even in competition with each other (BOJE, 2001; VILLAR; ROGLIO, 2019).

With no intention of "immobilizing" the spectrum of clinical research, our gaze turned to the scope of a bill for the creation of a law in progress in the Brazilian National Congress, which aims to create a regulatory framework for clinical research with the promise of profound changes in the relations of the actors in the system.

However, what we observe and advocate since the beginning of the contact with the empiric material is that the mere creation of the bill of law affected and was affected performatively by the various actants participating in this process. It was clear that descriptions add to reality (MUNIESA, 2014), and it was our aim to describe the performative way in which this dynamic was developed.

We then monitored the progress of the Senate Bill (PLS) No. 200/2015, which was later converted into Bill (PL) No. 7082/2017, still in progress until the closing of this thesis.

PL7082/2017, as it will be called hereinafter, contains several proposals sensitive to clinical research activities, with emphasis on: (a) restructuring the process of regulation of the ethical instance of clinical research by assigning new statuses to the CEP/CONEP system and by the creation of a new "National System for the Ethical Review of Clinical Research", (b) the regulation of the use of placebo in research protocols; and (c) the proposal of sponsors being obliged to fund post-experimental treatment for research participants.

We focused our attention on the struggle around the reformulation of the CEP/CONEP system (item "a", above), considering the complexity of the topic, the organizational discussions that this proposal entails and the level of contention that generates a large amount of available data for analysis.

2.4 Justifications, problem and research objectives

The novelty of this work is the explanation of the meta-organizational regulatory dynamics involving an ontologically flexible approach and employing a performative mentality that will allow us to see action from a post-human or socio-material perspective.

From a theoretical point of view, contribution is expected regarding how performativity is verified from intra and inter relations that constitute the regulation of the Brazilian clinical research, predominantly associated with a static and stabilizing phenomenon, but which in this thesis will be understood as a social-technical, relational and procedural artifact.

From a practical point of view it is expected an overcoming of supposedly dualistic movements of macro-micro, stability-instability and subject-object relations that can be discussed once again, promoting a new ontological perspective for the concept of organizational process, especially regarding the relativization of human intentionality or causality based on deliberate actions, in order to establish the naturalization of the performativity of network-actors in organizational processes.

From a methodological point of view it is expected that the use of cartography of controversies (VENTURINI, 2010a) is disseminated as a technique that enables the description of processes of constitution of realities in motion.

After these considerations, we announce the following research problem: "how to understand the regulation of the clinical trial segment in Brazil, from a procedural and performative perspective?"

Since, the main objective of the research will be to understand the processuality and performativity of the regulation of the segment of clinical trial in Brazil, we also detail specific objectives that guide the achievement of this work:

a) Conceptualize regulation, based on the experience of Brazilian clinical research from a procedural-relational ontological perspective;

b) Discuss regulation in their procedural and performative aspects as an agencement or socio-technical phenomenon resulting from the work of heterogeneous networks, arising from the regulatory process that acts on clinical research and which has been discussed in the context of a legislative process in progress through PLS 200/2015 and PL 7082/217;

c) Disseminate the cartography of controversies as a technique that enables the description of processes of constitution of realities in motion.

In this thesis, the phenomena will be examined following the methodological steps recommended by ANT. As Latour (2005) asserts, we want to follow the actants, identify the controversies that arise and unfold along the way, the stabilizations that also occur during the

process, and perceive, in the end, how the translational movements of reality that are being constructed for the Brazilian clinical research occur.

We believe it is possible to investigate these ways of ending the controversies that characterize the associations between actors-network, defining translations of interest, according to the methodological rules and principles advocated by ANT on how the propositions and arguments that substantiate the regulatory decisions are stated and constituted.

We will not fail to consider the descriptive way of how reality is constructed based on networks of symmetrically considered heterogeneous elements, and how this reality can be understood from a performative perspective.

We will assume the organizations involved in the research as continuous, precarious and partial collective aggregates, whose process is permanent and generates more or less stable effects, without giving up the “organizing” being taken as a verb (COOPER, LAW, 1995).

The organizations, or their emerging meta-organizational system, involved, including the CEP-CONEP system, will be the result of continuous, practical, complex and heterogeneous relations whose ordering will always be considered as "in formation" (ALCADIPANI, HASSARD, 2010). Therefore, it will not be the meta-organizational system of clinical research that will explain something, but it will have to be explained instead.

The thesis report is organized in seven chapters. In addition to the memorials and this introduction, I present the third chapter with a theoretical framework on the actor-network theory, which constitutes the theoretical conclusion adopted in the project. In the fourth chapter I present a theoretical review about regulation process. In the fifth chapter I analyze the performative approach, which will bring the questioning of the thesis in its onto-epistemological contour that aims to reframe the understanding of the dynamics and practices of an economic segment and the regulatory process related to it. In the sixth chapter, I describe the Brazilian segment of clinical research in its regulatory interactions triggered by the controversies that cause the dynamics of the sector and its performativity. The seventh chapter describes the methodological process, emphasizing the technique of mapping controversies as chosen to describe the performativity of the regulation process. In the eight chapter I describe the narratives of interest in the thesis used to assist in the theorizing process. In the ninth chapter I present the thesis of regulation as an actant, of an ontologically procedural nature, which performatively enacts the strategic actions it intends to regulate and suffers the same effects. In the tenth, and last chapter, I present the final considerations, when the problem and the research objectives are revisited, followed by the report of theoretical and managerial contributions, as well as recommendations for further research.

3 ACTOR-NETWORK THEORY

In this section I present the framework that constitutes the theoretical-empirical basis for the construction of the thesis proposal: the actor-network theory.

The Actor-Network Theory, or Sociology of Translation, originates from the sociotechnical studies of the "Science, Technology and Society" (STS) school, and gained great prominence from the works published by Bruno Latour, Michel Callon and John Law, seminal authors who started an alternative movement to try to understand reality from a procedural and heterogeneous view (CAMILLIS; ANTONELLO, 2016).

Among the seminal studies, the works published on microbes and the pasteurization process (LATOUR, 1984), on types of mollusks, known as scallops (CALLON, 1986) and on Portuguese caravels (LAW, 1986) stand out. that in all these works, humans interacted with technologies, with living organisms or with objects, demonstrating a new way of understanding reality based on the association between humans and non-humans, in a procedural perspective of flow.

The expression "Actor-Network Theory", and its acrostic "ANT", both coined by its main proponent, raised important self-criticisms that help us to understand the approach. Bruno Latour (1999), in his article "On recalling ANT", criticizes the four elements of the expression in order to justify, in the end, why he would survive the criticisms he formulated.

First, the definition of network, which cannot be taken in its "technical sense", as in the case of a pipeline or an internet network. The metaphor of the "network" has its own meaning, whose term comes from Diderot, who used it with the aim of avoiding the division between matter and spirit (LATOUR, 1996; 2019). The network is used to describe essences: instead of surfaces or spheres, the topology is changed to think of filaments or rhizomes, in the sense of a tubercle or root (DELEUZE; GUATTARI, 1987).

Second, the term actor, which in the Anglo-Saxon tradition, is considered a human and intentional agent, is criticized by ANT. In its place, the term "actant" is coined, designating humans, animals, objects or concepts (d, 2005).

Actor is an actor-network or a network of actors that cannot be seen as a source of action, but the moving target of a vast set of entities that nest towards it (LATOUR, 1996, 2007, 2010). An actor will always be an effect generated by a network of heterogeneous materials with which he interacts (LAW, 2004). The action is not seen as a consequence of a previous action, but as property of associated entities that result in a process of translations, connections and negotiations (LATOUR, 1999).

Third, the inclusion of the hyphen in the hybrid "actor-network" serves to deny a false understanding of a possible duality between actor and network, since what we intend to demonstrate is precisely that actors are not just actors, and networks are not “a piece of matter in the hands of third parties” since the actors are elements that integrate the networks themselves (LAW, 1992; LATOUR, 1999).

The hyphen should be taken as a mathematical sign of “equal”: actor = network or “actores sive reticula” (LATOUR, 2010). Thus, it can be stated that the hyphen is not intended to connect two halves of the expression (actor and network) but to negate them (neither actor, nor network). The actor or the network is not assumed to be entities or structures defined by properties independent of the relationships that connect them (VENTURINI, 2015).

Fourth, the term “theory” is also criticized. Latour (1999) and Law (2004), even states that ANT is not a theory but an empirical view of post-structuralism, which would be operationalized by actor-network translations (DUARTE; ALCADIPANI, 2016).

By the way, Latour (1999a), in another article in which he responds to the criticisms made by David Bloor (1999), even suggests that ANT should be seen as an analytical model to understand reality, without the pretense that ANT constitutes reality itself.

Therefore, the survival of the term was unusual, which in the end was due to the acrostic perceived by Latour (1999). “ANT”, as an insect, also would be representative of the meticulous work of data collection and analysis to describe social dynamics (LATOUR, 1999).

ANT represents an alternative approach to understand reality that relies on four approaches that embody it. In ANT, the alignment with the approaches of relational sociology (EMIRBAYER, 1997), processes (LANGLEY AND TSOUKAS, 2016), performativity approach (AUSTIN, 1962) and socio-materiality (ORLIKOWSKI, SCOTT, 2008) stand out.

The influence on a lack of interest in an anticipated definition of the object stands out from the relational sociology (EMIRBAYER, 1997). There is a relegation of an “a priori” labeling and an emphasis on tracking the propagation and reiteration of relational configurations (LAW, 1992).

The rejection that collective entities are conceived as stable and singular stands out from the process approach, as well as the defense that they are the result of elements continuously gathered (LAW, 1994).

The performativity approach, originated by Austin (1962) emphasizes the effect of language not only as descriptive, but as a promulgator of reality. Callon (1998) recognizes it in his analysis of economic models whose theorizations would not only describe pre-existing

conditions for the occurrence of economic phenomena, but would have the effect of interfering with their conditions.

Considering the relational, procedural and performative influences on ANT, the notion of a reality must coexist with a certain manifestation of standardization that generates fixation and stabilization (LATOUR, 2005), since it would be implausible to conceive in fluid institutes without a minimum of substantiation (CABANTOUS AND SERGI, 2018), a phenomenon known as 'punctuality', which is a simplifying effect of the complexity of networks (LAW, 1992).

Finally, ANT is also influenced by socio-material approaches that touch on the principle of symmetry or the recognition of an ontological status between humanity and objectivity (TONELLI, 2016).

I present bellow some of the main concepts needed to understand ANT.

a) Symmetry

The development of the notion of symmetry, originated in David Bloor (1976), started from the critique that elements of nature and society were not being symmetrically considered to explain between true and false sciences. Bloor (1976) defended the impartiality between true and false, between rational and irrational, between success or failure, in addition to the need to transfer the right of explanations to the then neglected pole of society. Faced with criticism by Latour (1999), who considered Bloor's model still asymmetric, Callon (1999) developed the notion of generalized symmetry according to which a true symmetric explanation could not start from any of the poles (nature or society).

Callon and Latour's concept advanced to refer to symmetry, not only as an equal treatment between truth and falsehood in the history of science, but also to establish an ontological symmetry between elements of nature and society and between humans and non-humans for the generation of negotiations and performativities (TONELLI, 2016).

Therefore, symmetry has become a heuristic tool used to understand the contingent role played by actants within an actor-network (CALLON, 1999) based on the assumption of complete heterogeneity between the elements of nature and society (LATOUR, 1994).

b) Social

The peculiar and essential meaning given to the term “social” by the authors of ANT is remarkable. While we refer to "social" as a phenomenon that is in a situation of stability or something that is "already aggregated", for ANT the "social" cannot be conceived as if it were a domain, attribute or quality to the extent of playing the role of offering a “social explanation” to some other state of affairs (LATOUR, 2007). For ANT, therefore, the allusion to “social factors”, “social structure”, “social practice” or “social dimension” should be questioned as they are under construction,.

According to Mol (1999), reality does not precede the practices through which people interact, but is shaped by them. Thus, the notion of “social” needs to be explained and, therefore, redefined, seeking to understand the content of what is “aggregated” under the aegis of a society.

It appears that the mainstream of sociological thought, of Durkheimian conception, is challenged by ANT, as not only the words “social”, but also the very definition of “science” are deconstructed by Latour (2007), as they are considerably unstable entities to question even if it is possible to conceive the strength of a “socio+logy”. For this reason, Latour (2007) proposes a redefinition of the object and methodology of the “social sciences”. Thus, by rejecting the assumptions presented above, Latour proposes to adopt as an enigma to be solved what the Durkeimian view considered its solution.

The table below summarizes the main distinctions between what Latour calls “social science” and “association science”, the latter representing ANT's thinking:

Table 1 Difference between social science and association science

Social science	**Association science**
• It sees social groups as an element capable of shedding light on residual aspects of economics, linguistics, psychology, administration and law, among others	• Considers social aggregates as something to be explained by specific associations provided by economics, linguistics, psychology, law and administration, among others.
• The social is a homogeneous thing	• The social is a series of associations between heterogeneous elements (from chemical bonds to legal bonds, from physiological organisms to political parties)
• The social designates a thing (like a black sheep among white sheep)	• The social designates a type of connection between things that are not social among themselves.
	• Any kind of household; it can be social
• It is pre-relativist	• It is relativist
• They consider that the main characteristic of the social world is to recognize, regardless of who draws them and with what tools, the unquestionable existence of the borders that separate one from the other	• The first characteristic of the social world is the constant effort of some people to draw borders that separate them from others

• Considers its role to stabilize a group	• Considers its role to map the controversies surrounding the formation of groups

Source: Latour (2007), adapted by the author.

Finally, according to Tureta and Alcadipani (2009), the empirical-realist character of ANT is related to the idea that it is possible to analyze actors-networks that perform practices and processes, even if, at first it is difficult to know what/who makes things happen or people act, which reinforces the view of Latour (2007, p. 53) when he states that "the presence of the social needs to be demonstrated recurrently".

c) Controversy

Controversies are central to ANT (CALLON 1989), as associations between heterogeneous elements occur under friction. They are also considered one of the most complex phenomena to be observed in collective life (VENTURINI, 2010a), although little explored among the authors of ANT. It involves anything that challenges the status quo among actors (HUSSENOT AND MISSIONER, 2010).

As a way of developing controversy studies under ANT, Latour created MACOSPOL (Mapping Controversies on Science for Politics), a project funded by the European Union to develop a collaborative platform for mapping controversies under the actor-network approach.

According to MACOSPOL documents (2007, p. 6), controversy is referred to as every piece of science and technology that is not yet stabilized or closed. This definition presents controversy as a state of shared uncertainty about facts of scientific nature. Venturini (2010a) elucidates some important features to understand the controversies in the ANT approach.

First, any actant can participate in a controversy. They can involve human beings or groups, but also non-humans, integrating "heterogeneous arrangements" (LAW, 1999). In this list in which elements from different worlds can integrate it, there are people, natural phenomena, industrial and artistic products, economic institutions, scientific artifacts and so on.

We are not claiming that an object has a volitional capacity like that of a human, but that human action does not result exclusively from the will dissociated from the relationships it has with objects.

Unlike classical sociological approaches, ANT does not seek a vision based solely on the interests that involve a fact to explain it. The dispute of interests and the explanation through

“contexts” would be insufficient to understand the production of facts, and should not be taken as a determining factor in this production (LATOUR, 2007).

Every volition is manifested from symmetrical relationships in which any human or non-human actant is present, which makes them protagonists of controversies that function as a “hybrid forum” (CALLON; RIP, 1992) or a space of conflicts and of debates and negotiation in search of stabilization.

Second, it is controversies that display the formation of the social in its most dynamic form. From them emerge alliances, coalitions, subdivisions and multiple forms of associations (VENTURINI, 2010a) so that actors can, at any time, associate or dissociate themselves from networks of controversy (CALLON, 1989). The notion that collective life is made up of alliances as well as their dissolutions also emerges here, thus emphasizing the role of controversies in the constitution of the social (VENTURINI, 2015).

Third, controversies are resistant to reduction. This means that practically everything gives rise to discord, which is consistent with the rhizomatic view of ANT, as if there were an infinite regression that makes its closure impossible. Even the formulations of the questions would be subject to controversy, to the point that the actors not only disagree with the answers, but they don't even go so far as to agree with the questions (VENTURINI, 2010a).

Volcanic magma, which alternates between its liquid and solid states, is a good metaphor to illustrate the dynamics of controversies, which ceaselessly settle down or intensify (VENTURINI, 2010a).

Fourth, controversies are the object of discussions that are not always verbal and arise when ideas and things taken for granted begin to be questioned and debated. The greater the disagreement, the deeper and more expensive the controversy will be, which will demand the ever-greater work of more actors to serve as allies to the positions taken in the hybrid forum (NOBRE; PEDRO, 2010).

The solidity of a controversy is an effect of an alignment between allies articulated in defense of an argument submitted to rebuttal, in the sense that new elements will act to convince the allies to change sides and betray the argument that presents itself as a fact (LATOUR , 1999).

Fifth, controversies represent conflicts (VENTURINI, 2010a), and although the concepts for referring to conflicts as specific situations are distinguished, controversies would be process-oriented notions (HUSSENOT, 2008). In this work, we understand that conflicts can also be relational (SIMMEL, 1904), and in this sense the terms “conflict” and “controversy” will be taken as synonyms, in an approximation with Venturini's position.

Controversies may vary in degree and may represent trivial or serious issues, depending on the number of connections involved by the actors-networks and the distribution of power resulting from them (LATOUR, 1981).

As criteria for choosing a controversy, Venturini (2010a, 2010b) and Hussenot (2014) suggest that it is advisable to investigate where collective life becomes more complex, where the largest and most diverse variety of actants are involved, where alliances and oppositions are transformed in a more irrational and inconsistent way, where nothing is as simple as it seems, where everyone is screaming and fighting and where conflicts become more severe.

The closure of a dispute constitutes what ANT calls the "black box", a cybernetic term that means the concealment of the internal systems of a system, or the result of an attitude of making opaque the functional processes that transform one data into another (LATOUR , 1999).

A black box is formed, or a statement becomes solid as a fact, whenever it is introduced in new formulations as an unquestionable premise, to the point of deducing that the solidity of a fact, or its stabilization, will always depend on all those who keep it moving, in a work of legions of allied and interconnected networks (LATOUR, 1999).

Whenever a fact encounters opposition or obstacles in its circulation, it means that it will be pushed towards an assertion of "falsehood" in an environment of controversy in which black boxes will be reopened.

When a fact becomes a black box, it means that it has created an autonomy, an independence. When the black box opens, it means the reinstatement of controversy.

The emergence and the development of controversies occur simultaneously with the production of collective aggregates (or groups) that are placed in opposition to each other, which are accompanied by elements enlisted to support their positions and arguments that delineate these group boundaries, enabling the construction of analysis maps of the established relationships. The controversies will be perceived as a result of these different senses of belonging of the groups and of the translations that are formed from this work of the actors-networks.

d) Power

Once the complete symmetry in the recognition of agency has been established between heterogeneous elements that combine to constitute actors-networks, as well as being explained that such associations are driven by a friction process characterized by a continuous movement of controversies, ANT proposes to elucidate how the dynamics of these associations that weave

reality are processed. Therefore, it is necessary to consider the power arising from these network associations, as a necessary step to understand how controversies are punctuated and procedural realities are provisionally reified.

According to ANT, power is not something triggered by an initial impetus, nor held or accumulated by someone, but it is a consequence, and not the cause, of the collective action (LATOUR, 1986).

Latour denounces a tautology when it is said that a dictator or an organizational manager is obeyed because they conquered or held power, as this does not refer to something that someone holds or will accumulate, but is always a composition made "by others". Power is born from relations, being always in association with something or someone, and does not precede them (LATOUR, 1986).

It can even be said that the concept that ANT confers to power demonstrates that it is not something crucial to this approach, but the completely uneven perspective it has in relation to modern approaches of power justifies its reference.

Latour (1986) denounces a paradox: if someone simply holds power "in potentia" nothing will happen, but if you exercise it ("in actu") then it will be others who will perform the action, not this someone who supposedly possesses it.

According to Latour (1986), power does not explain action, but needs to be explained by the action of others – those who obey the dictator or the organizational manager, for example. This is because if the notion of power could be used to synthesize the consequence of a collective action, it would not be able to explain what sustains it.

In his famous article "The power of association" (1986), Latour describes some ways of dealing with power as an effect rather than a cause.

First, he makes a distinction between the diffusion model (derived from a sociological conception based on the recognition of the social, with a modernist slant) and the translational model (derived from ANT, which is also known as the sociology of translation).

The "diffusion model" represents a perspective that recognizes a dualism or separation of interest groups that distinguish science and technology, on the one hand, and society, on the other. This vision, which marks modern thought, would have artificially created incommunicable spheres of agencies, making it impossible for facts, machines and people to associate, giving rise to a notion of "social determinism" and "technological determinism" that would not be able to interact.

In the "translation model", heterogeneous chains of associations are recognized, which create mandatory points of passage between people, facts and machines.

Figure 1 Diffusion and Translation Models

Diffusion Model **Translation Model**

Source: Latour, 1999

Thus, under the diffusion model, “power” is understood as a phenomenon endowed with an internal and inertial force whose displacement does not need to be explained, except for its deceleration resulting from the action of other people.

Latour exemplifies that technical progress is usually explained in this way. The steam engine, electricity and computers are endowed with an inertial power that can hardly be stopped except by reactionary groups who try to impede such progress. Latour refers to fashion, ideas, products and lifestyle patterns, as endowed with the same inertial force that spreads through society without the need of an external drive.

Therefore, the diffusion model would define power based on three elements: (a) the initial force that triggers the movements and that constitutes its own energy; (b) the inertia that preserves this energy; (c) the medium or “tokens”, through which the phenomena circulate, and which manifests the frictions or resistances that might increase or decrease the propagation of this power. From this point of view, when someone observes an order being given by a manager to two hundred people, it is concluded that the force that mobilizes such people is in the hands of that manager. According to the diffusion model, everything could be explained from this inertial force or the resistances used by these “tokens”.

The alternative view proposed by Latour (1986) is based on the translation model. This model recognizes that the propagation of anything in time or space is in people's hands. For this model, there is no inertia to explain the propagation of a phenomenon, whose energy is not intrinsic to it, nor where it can be accumulated or capitalized. For a phenomenon to move, it will have to find this energy at all times, through the associations maintained with different actors that interact with each other.

The initial force is no longer responsible than any other, nor is it transmitted in its wholeness, besides depending on the actions of those closest to it along the chain. Rather than

a passive means by which force is exerted, the members are active, changing and shaping phenomena as it moves. Instead of transmitting the same phenomenon (deviated or accelerated by friction), what happens is that there is a transformation of this phenomenon in a clear reference to the notion of performativity.

Obeying an order given by someone would require the alignment of all the people involved, who would faithfully agree with it, without adding or subtracting anything. In fact, the given order is modified and composed of several actors who slowly move towards something different towards their own goals.

Latour (1981) then points out that power is always an illusion that people have when they are obeyed because, in fact, it is made up of the will of others, and not of a supposed leader.

It can be noticed that Latour denounces the convenience of sociologists of the diffusion model in explaining the power of a dictator through intrinsic and inertial attributes. It would be enough to say that such a person has a lot of power, but in the translational model the origins need to be explained, as well as the very concept of the social, which cannot be taken a priori. Power will always be something provided by the pre-existence of society or something that has to be obtained by enlisting many actors.

Since society is not made before our eyes, it is then unable to explain our behavior, but it is instead shaped by our collective action. This does not imply that we have to deny the existence of a comprehensive society, but change the ostensible model to the performative model of understanding the society (LATOUR, 1981; 1996).

Societies are not a reference for an ostensible definition of discoveries, but are performed through the efforts of all who comprise them. The “principles” of constitution of society give way to “practices” whose participating elements are social and material.

Here it could be exemplified that the “power” of a manager would be conquered thanks to a series of phone calls, record keeping, walls, clothes and machines, and here the symmetry of heterogeneous elements for their formation is also evidenced.

Likewise, the power of a statesman would be supported by the symbols of a nation, an anthem, flag colors, liturgies and other signs that support that claim to power, fueled by social and material elements.

Therefore, the formation of collectivities, which occurs through the inscription or enlistment of micro actors who start to act as if they were an individual will, occurs due to forces that are not "held" by the macro actor, but stem from those with whom they associate. (CALLON, LATOUR, 1981; ALCADIPANI, HASSARD, 2010).

e) Translation

If controversies represent situations of disagreement between heterogeneous actors engaged in action (VENTURINI, 2010a), the translations will seek to establish their contradictory interests (LATOUR, 1999), reshaping network actors and causing them to appear, change or be excluded from reality (HUSSENOT, 2014).

The notion of translation was created by Michel Serres, one of the great influencers of Latour's thought. Serres (1996), who also defended a practical impossibility of dualism between the sciences and the outside world, developed the notion of multitemporality by stating that the phenomena of reality refer at the same time to the past, present and future (TONELLI, 2016) .

These ideas outlined what translation consists of in the view of Michel Serres (1996), which are processes of building connections, passages or establishing communications, an act of invention or *bricolage* that emerges from the mixture of heterogeneous multitemporal elements (TONELLI , 2016).

This notion of translation did not only have linguistic or symbolic connotations, but involved acts of displacement or substitution of knowledge, people or things, and fell not only on elements that it translated, but also on what was translated in a clear allusion to the performativity of relations (CZARNIAWSKA, 2005).

The notion of translation was incorporated by the seminal authors of ANT, who defined it as an "interpretation given by fact-makers to their interests and those of the people they enlist" (LATOUR, 1998). It was later conceived as a geometric notion of displacement and transformation, which offers new interpretations of interests, channeling people into different positions (LATOUR, 1999, 2007).

Duarte and Alcadipani (2016) explain translation as a process of combining several interests, which were then distinct, in a single composite objective. They point out that this association, which takes place from various entities that form a "macro actor", makes it relatively stable, but reversible, relational and supported by the configuration of networks, as a result of the momentary association and not inherent to its components.

According to Latour (1999, p. 198), translation can occur in five ways:

First, Latour (1999) states that considering that people are necessary to transform a statement into a fact, one way to co-opt them would be to adapt the object of the statement in such a way that it meets their explicit interests. Here, Latour refers to a simple search for convergence of interests, something corresponding to the idea of "capturing", which consists of taking positions in less controversial arguments, with simpler black boxes, and only later

raises the most relevant controversies. Latour (1999), however, warns that this search for convergence can excite followers.

He then mentions that when Pasteur produced the vaccine against cholera in birds, he aroused so much interest of other groups that it was believed that this would be the solution for all infectious-contagious diseases in men and animals. He then claims that if on one hand indifference must be overcome, on the other hand sudden enthusiasm must be curbed. This movement is called by Latour as "translation 1", whose figure is represented below:

Figure 2 Translation one: I want what you want

Source: Latour (1998, p. 181)

Second, Latour (1999) points out that another way to align the interests of people who are not expected to have a natural convergence is to create roadblocks to these people's paths, making it imperative that they then redirect their efforts in a way that converges with theirs or with the author of the scientific thesis (LATOUR, 1999).

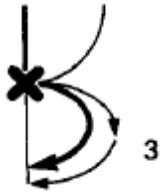
Here, the example is of the wealthy merchant who wanted to invest resources to study the origins of men's logical abilities. Scientists found the idea unfeasible, but included it in their goals and obtained the merchant's resources to proceed with their agenda. Thus, the scientists did what they wanted with the merchant's money and not what the merchant intended in the beginning. A millionaire, in turn, agreed to take on the scientists' interests, hoping that his would also be considered. This would be the example of translation n. 2, represented in the figure below:

Figure 3 Translation two: I want it, why don´t you?

Source: Latour (1998, p. 181)

Latour (1999) adds a third translation by demonstrating that small deviations can keep convergent the interests of the scientists and of the enlisted people. Therefore, it is necessary to recognize the blockage on the main road, see a well-marked detour and control the detour so that it is small. He mentions the example of early twentieth-century architects who were building stronger and stronger warships using a lot of steel. However, magnetic compasses caused these ships to get lost in the ocean. The controversy then was either to use less steel or give up magnetic compasses. A small detour was necessary to close this "black box", and so those involved gave a chance for the development of a new technology, which was the gyrocompass. Translation n. 3 is represented below:

Figure 4 Translation three: if you just make a short detour...



Source: Latour (1998, p. 181)

A fourth translation is presented in cases where the interests at stake are not as explicit as in the previous situations. Latour (1999) presents tactics such as shifting goals, inventing new goals, inventing new groups, and becoming invisible.

I reproduce Latour's example to help illustrate this modality of interest translations: a journalist, in the late 19th century, published that in a certain battle, the French had been defeated by the Germans because the latter would be healthier (this would be the first translation into a version of the military defeat of the French). The journalist went on to say that the better health of the Germans was due to their superiority in basic sciences (second translation). He also explained that science was superior in Germany because it had a more solid basic education (third translation). At the end, he informed the reader that the French Assembly, at that time, was cutting funding for the basic sciences. This contributed to a fourth shift: no French military recovery would be possible without money, since there is no science without money, there are no healthy soldiers without science, and there is no French recovery without soldiers. At the end, the journalist suggested that each reader wrote to his deputy, pressing him to change the vote in order to ensure that the budget for basic science was not reduced.

From this example, the intention to take up arms and rescue the honor of the French army came to mean "write a letter to your deputy so as not to reduce spending on basic science"

(LATOUR, 1999, p. 193). A slow, narrow-ranged move to “tie them up” into broader problems has taken place. Translation n. 04 is represented by the figure below:

Figure 5 Translation four: reshuffling interests and goals

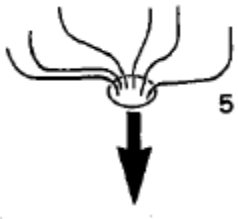
Source: Latour (1998, p.199)

Finally, Latour consolidates the four modalities of translations to consolidate them in the fifth one, which would be a summary of all these movements: (a) serve the interests of others, (b) convince them that the paths trodden are blocked, (c) attract people to small deviations and (d) invent new groups or goals and derive interests.

Therefore, among the tactics of translation in which the interests at stake are not so explicit, the notion stands out that the recruiter must be guaranteed to maintain control over the merits of their assertions. Latour (1999) mentions the case of Napoleon, who is attributed the feat of winning major battles, although it is known that the war was won by half a million people under his command.

As in the case of Napoleon, there would be, therefore, another attribution distribution process that would only be explained by means of another type of translation that allows the author to assert himself as indispensable in the process. So the thesis author would no longer be a container and would help them to promote their own interests. Controversy becomes a controlled process of convergence. This translation that consolidates the previous ones is represented in the figure below:

Figure 6 Translation five: become indispensable



Source: Latour (1998, p.199)

Callon (1986, p. 203) defined translation as a “process during which the identity of the actors, the possibility of interaction and the margins for maneuver are negotiated and delimited”. This negotiation process involves four movements: problematization, interessement, enrolment and mobilization.

In the problematization movement, the main actors establish their identities and their goals to create a mandatory crossing point that everyone must accept in order to achieve their interests. It is as if the rules on how controversies will be developed were established (CLEGG, 1989). The interessement involves the imposition on other actors of the movements defined in the problematization, preventing the identities defined in the previous phase from being lost. Enrolment means defining the roles to be played by the actors and how the others will relate within the networks. In the mobilization phase, there is a coalition in which the main actors borrow the strength of their allies, passive agents, and become their representatives or spokespersons. At this stage, dissenting voices are silenced and the controversy ends with the commitment to negotiation, the result of which becomes legitimized.

Law (2007) defined translation as a process of minimizing controversies, but also compared it with the notion of betrayal (2003). He stated that the notion of translation refers to the similarity or reliability of what was translated, while betrayal refers to the difference that transforms, which is exactly the performative aspect verified in the understanding of translation emphasized by ANT.

Latour, when publishing his work “Science in Action” in 1987, referred to ANT as the “Sociology of Translaction”. In 1989, the French version of “La Science en Action” brought the term “Sociologie de la Traduction”. The Brazilian edition was translated from English in 1998, with references to the “sociology of translation”, making the expressions 'revolution' and 'translation' synonymous, differently from what was defended by Law (2003).

3.1 How facts are constructed under ANT

Latour's recommendations are presented in his work, “Science in Action” (1999), in the form of methodological principles and rules necessary for the construction of scientific facts. In the next section, we will address the sources of uncertainty presented by Latour in his work “Reassembling the Social” (2007), during the course of the construction process of the “social”.

These sections reinforce the theoretical framework to understand ANT. On the other hand, they also contribute to the understanding of the methodological process employed in the elaboration of the thesis.

The work “Science in Action” (1999) has the great merit of providing a descriptive-analytical guide on how controversies are raised and stabilized, how the social is constructed or how reality is reified. This guide is operationalized through seven methodological rules presented and analyzed below.

a) Latour's first methodological rule

> We study science in action and not science or ready-made technology; for this, either we arrive before facts and machines have turned into black boxes, or we follow the controversies that reopen them. (LATOUR, 1999, p. 421)

In the scientific process, what is studied is “science in action” and not “ready-made” science or technology. Entry into the world of science and technology is through the “back door”, “science in construction”, and not “finished science” (LATOUR, 1999).

Therefore, it is necessary to monitor “controversies” up to the point that with their dissipation “facts and machines” become “black boxes”.

Below are some observations relevant to the understanding of this methodological rule:

The first one is the reaffirmation of the ontology of flow, which does not consider the scientific fact as ready or finished, but considers it the precarious result of a stabilization through the closing of controversies upon the creation of black boxes.

Second, I find that even the black box cannot be considered as finished, as controversies are recurrent. In this sense, it is worth to consider that the idea of “change” does not receive from Latour the importance of what is known in the mainstream of “sociology of the social”, since it is not an exogenous or incidental phenomenon, but rather a constitutive element of reality itself, procedural by definition.

Third, Latour does not compromise with the exclusive notion that the black box means the cessation of controversy for its pacification; instead, it can be closed due to impossibility or exhaustion, given the complexity involved. That is the reason why only inputs and outputs are often described without specifying the intermediary paths along which the dynamic develops. The idea is to close the box, paint it black and say that the issue is resolved, even though this is not always the case.

Fourth, Latour emphasizes the inductive character of the scientific process. He recommends that in the search for knowledge of a science in action, it is necessary to “leave [aside] knowledge about knowledge” (LATOUR, 1999, p. 78). He would be defending a move away from the presupposed view of what constitutes knowledge in order to conceive the simple process of describing all the elements that are contributing to the phenomenon, which implies

saying that both people and objects contribute to the emergence and closure of controversies and act on reality.

Still on this matter, Latour even questions the deductive positivist view that a starting point, a “framework” or a theoretical framework to understand reality would be necessary. Latour will say: “Simply describe the facts that are at hand” (LATOUR, 1999, p. 94).

Latour also states:

> “If X is a mere ‘case of’ Y, then study Y, […] since X would not teach anything new. If something is nothing more than an example of a general law, then study this general law directly… a case study that needs to be complemented by a framework is a case study, already at the outset, poorly chosen ” (Latour, 2004, p. 5).

Fifth, one cannot fail to notice in Latour the defense, although implicit, of the principle of symmetry between the interactions of humans and objects to capture all the existing controversies that are acting for the constitution of the intended reality intended to be stabilized as scientific truth.

In this case, the view of heterogeneity is evident in this view. Latour incorporates elements of people's daily lives, but which occur inside scientific laboratories, to demonstrate that they also contribute to the establishment and closure of controversies: scientists also have problems such as "deadlines", "suspensions", "moves" that are elements that are not present in the imagination of what would represent a scientific process.

b) Latour's second methodological rule

> To determine the objectivity or subjectivity of a statement, the efficiency or perfection of a mechanism, we should not look for its intrinsic qualities, but for all the transformations that it undergoes later, in the hands of others (LATOUR, 1999. p. 420).

Based on this second rule, Latour (1999) also enunciates a principle: that the scientific process is a collective work, never an individual one. A scientist who doesn't get involved with others, does not interact, does not share the results and does not submit his propositions to external scrutiny is a contradiction by definition.

Latour argues that the way facts are arranged in a proposition leads people to take very different paths; therefore, the greater the debate around the claim, the more evident it becomes that it has been subjected to different zests, until the controversy is over.

I dare to say that this is an idea analogous to the process of refining a precious metal, such as gold, which becomes purer when subjected to extremely high temperatures. This submission

of a proposition to controversies is what will measure the extrinsic quality of the assertion intended to be stabilized.

In this sense, it is relevant to observe Latour's words: “the fate of the things we say and do is in the hands of those who use them later” (LATOUR, 1999, p. 130). And the quality of these statements or achievements will depend on the level of contention to which they are submitted.

Latour even surprises common sense, if we compare it with the predominant thinking of “social theorists”, of modern matrix, who defend the dualism between politics versus science. This is because Latour, on the contrary, associates the scientific spirit with “noise, heat and passion”, unlike the behavior of common men, whose daily life would be represented by “silence, coldness and rationality”. Latour says: “The more discordant, the more scientific and technical the literature becomes” (LATOUR, 1999).

Latour (1999) presents some instruments to handle controversies, which are rhetoric, endorsement, stylization, stacking, framing, staging and capture.

Regarding rhetoric, it is interesting to notice once more the mark of heterogeneity implicit in Latour's thought, which turns the scientific and political process into something similar to “Siamese siblings”, demonstrating the monism and symmetry of their associations. Once again, common sense is challenged: quite contrary to what appears to happen, the scientific process takes place around debates whose truth is claimed through authoritative arguments, through which, when friends are enlisted , one would be looking for the solidification of subjective opinions about objective facts (LATOUR, 1999).

Therefore, the scientificity of a proposition is not only attributed to refutable experiments, but not yet refuted (POPPER, 2007), but also depends on the endorsement of statements made by allies who lend their credibility to attribute truth and reliability to that proposition (LATOUR, 1999).

Just as an instance, imagine what would happen to a scientific thesis that was not published. Latour's answer is absurdly simple: nothing happens! Ostracism generates an emptiness, a "nothing". On the other hand, if we think about a perfect work that was published in a scientific journal with low credibility, the possibility of this work not even being noticed by the scientific community would be high. And, on this issue, Latour goes so far as to say that being criticized is worse than being ignored (LATOUR, 1999).

Thus, in order to avoid such situations, it is expected that the scientist submits his or her work to the most prestigious discussion forums possible. Therefore, after passing through the scrutiny of the criticisms made to it, the article will receive the authoritative endorsement of

peers, who will attribute to the fact the due relevance and visibility so that the black box closes. Possibly, from this point onwards, the scientific propositions arising from the scientist's work will be received as scientific facts.

Latour (1999) states that during this path contenders to the scientific thesis will appear, who constitute the beginning of the controversies necessary for the advancement of scientific knowledge. The contenders, in this case, will do everything to avoid recognizing the proposition as a scientific fact. And the tactic proposed by Latour is to weaken enemies (for example, also criticizing their own propositions), join with allies (for example, seeking convergence with other scientists) or even putting enemies to fight with each other (such as, for example, opposing two texts in such a way that one invalidates the other) (LATOUR, 1999). The point revealed by Latour here is that the scientific process is political, and that science is a collective work whose success depends much more on exogenous than on endogenous factors to be established.

Latour continues on his course of closing black boxes (or stabilizing controversies) warning that once the initial rhetorical phase is over, it is necessary to prepare for the future (LATOUR, 1999), since as the present proposition invalidated past theses, future theses will invalidate the current proposition, and it is thus crucial that a scientific proposition survives subsequent production. In this regard, Latour makes an analogy with genes, which also do not survive if they are not transferred to subsequent organisms (LATOUR, 1999). Therefore, it will be necessary to keep up with the citation of any scientific articles originated from subsequent works.

It is in this process that what Latour calls stylization occurs. The fact is reaffirmed countless times, but it moves away from its initial statement, and the statement is submitted to erosion and polishing by all who accept it to the point where that fact detaches from its author. In this case, knowledge, not only stabilizes but also becomes tacit. And here, Latour describes another way in which black boxes close (LATOUR, 1999).

Latour also presents a new strategy called stacking, which adds to the strength of rhetoric and argumentation, through which the search for stabilization would be in the power of nature and not only of politics.

Through stacking, the scientist must objectively show what there is in the text. The belief in the word of the author of the thesis should be reinforced by direct examination of the previous layers contained in the text, represented by figures, tables, data and graphs that appear in the text.

Then, Latour (1999) presents the framing strategy, which constitutes a technique to upon the immunization of the text against eventual and future criticism, the author considers that the readers are eclectic as to quantity of available resources to deal with the scientific proposition.

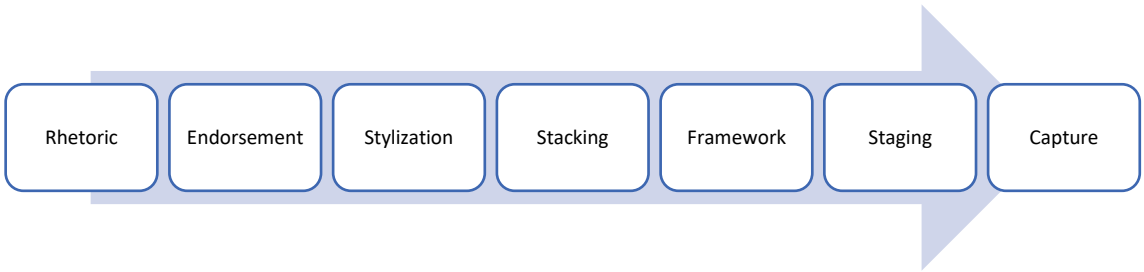
Thus, it is convenient to reduce both the intensity of the controversy and the resources used to support it, in order to propagate the thesis to a larger number of readers. The purpose of this idea is to show the thesis to a larger number of readers with the purpose of disseminating the fact that one wants to create. The aim is always to stabilize it. Thus, balancing the control of the depth of disputes would be the necessary strategy to improve this stabilization.

A new strategy presented by Latour (1999) is staging, which consists in the assumption of an imaginary reader, in a semiotic sense, asking what kinds of proof will be required to believe the author of the scientific proposition, which is translated by the anticipation of possible future criticism that the fact may suffer.

There is also the strategy of capture, which consists in ordering arguments that are better known and less easy to discuss as preceding more debatable statements. Thus, the objective is to arrest, involve, hold and persuade the readers by sharing the most converging ideas, and only then convince them about topics of greater controversy, since at this point they will already be captured, committed or hooked on the idea being defended.

The second methodological rule consolidated in Figure 2 shows the strategies presented by Latour to stabilize controversies:

Figure 7 Controversies stabilization techniques



Source: Latour (1999). Elaborated by the author.

Latour continues to build the scientific fact (and reality) stating that just as it is necessary to enlist people, it is necessary to control the behavior of these people, making their actions predictable (LATOUR, 1999).

Therefore, the process must be collective and coordinated to proceed successfully. It is at this moment that Latour addresses “translations”, a central theme at ANT. It must be stressed that the notion of translation presented by Latour (1999) has an ingredient of control and power,

since the transpositions or convergences of interests resulting from stabilization can be deliberated by the actants.

c) Latour's third and fourth methodological rules

> As the resolution of a dispute is the cause of representation of Nature, not its consequence, we can never use that consequence, Nature, to explain how and why a controversy was resolved (LATOUR, 1999, p. 420).

> As the resolution of a dispute is the cause of the stability of society, we cannot use society to explain how and why a controversy was settled. We must symmetrically consider efforts to list human and non-human resources (LATOUR, 1999, p. 420).

After describing and exemplifying the five types of translations, Latour (1999) resumes the topic of how to make predictable the actions of allies enlisted in the defense of scientific affirmation. His concern is clear in the examples:

> "(...) projects that arouse great enthusiasm are soon shelved; certain theories, which tried to infest the world, shrank and eventually became the fixed idea of some lunatic in an asylum; [...] undoubted facts are quickly transformed into fiction; [...] Consolidated industries, which seemed to have the capacity to last forever, suddenly become obsolete and begin to disintegrate, being replaced by newer ones" (LATOUR, 1999, p. 200).

He further states that "*discordants proliferate that interrupt the propagation of facts or artifacts*" (p. 204); and his recipe to avoid this situation is that control and predictability over allies will depend on enlisting other kinds of new allies: non-humans.

The possibility of expanding telephone lines by the Bell Company was only possible when the "electrons" were activated to amplify the signals, which made the lines transcontinental. Latour (1999) then argues that the Bell Company defeated rivals in the telephone industry when it entered into a partnership with electrons.

These non-human objects, new allies to the dispute settlement project, also need to be controlled. Latour proposes that this juxtaposed set of allies be transformed into a whole that acts with uniqueness through the construction of machines or artifacts.

The skills of engineers who multiply the methods that lead to this juxtaposition are then highlighted. Latour argues that in a manufacturing process, for example, "a piston is more reliable than a worker" (LATOUR, 1999).

Payment systems, error detection systems, cotton spinning machines and a standard worker who operates them are the consolidated result of a regularly functioning automaton tangle that results in a cohesion of actions that finally close the black box, and are represented

by the idea that several elements (human and non-human allies) are led in a controlled way to act as one.

Although the vision of a deviation in focus related to the construction of scientific facts appears and only then there is a concern about objects or artifacts, in reality Latour emphasizes that the construction of the "scientific fact" rigidly follows the same automation process by which objects and artifacts are associated with human action. Both represent the end of controversy or the closing of black boxes. (LATOUR, 1999).

Latour then consolidates his vision: the builder of facts must be concerned with a set of strategies to enlist human actors, but must also devise strategies to enlist and maintain non-human actors, the latter having the role of preserving the former (LATOUR, 1999).

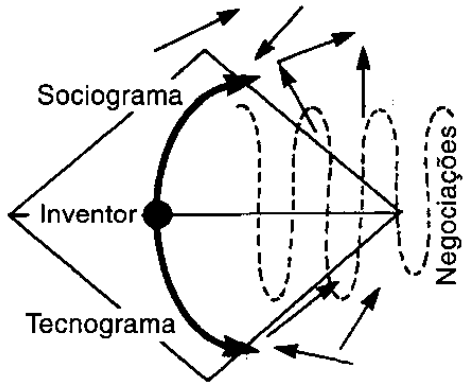
Thereby, one more principle is stated:

> "We are never faced with science, technology and society, but rather with a range of weaker and stronger associations; therefore, understanding what facts and machines are is the same as understanding what people are" (LATOUR, 1999, p. 423).

It is clearly perceived that there is an exchange of agencies between humans and non-humans in this process, and this joint and integrated vision is essential to understand the closing of the black boxes.

Once again, when defending his "translation model", Latour (1999) explains that the process of construction of facts (and artifacts), involving the agency of humans and non-humans, is explained through two systems of interdependent alliances that he calls sociogram and technogram:

Figure 8 Sociogram and Technogram



Source: Latour (2008, p. 230)

The sociogram reflects a set of strategies needed to enlist the supporters of the idea one wants to defend, which is done through rhetoric. The technogram would represent the strategies needed to control the behavior of these supporters, which is done by instruments or objects.

The aim would be to achieve as many associations as possible between the sociogram and the technogram. In these interactions, Latour (1999) demonstrates that the associations between the sociogram and the technogram actually mean countless interactions between things and people, clearly showing his defense of heterogeneity and the agency of humans and non-humans, which are valued postulates to ANT.

These associations of the sociogram-technogram relations are also a protection for both systems, so that one injunction relies on the other whenever negotiations over the controversy prove to be an obstacle.

Thus, by enunciating his third methodological rule and paraphrasing it in the fourth rule, Latour (1999) reinforces that efforts to enlist human and non-human resources in search of dispute resolution must be considered symmetrically.

d) Latour's fifth methodological rule

> As to what technoscience is made of, we must remain as undecided as the various actors we follow; whenever a divider between interior and exterior is built, we must study both sides simultaneously and make a list (no matter how long and heterogeneous) of those that really work (LATOUR, 1999, p. 422)

It has already been said that the scientific fact under construction is a collective elaboration formed by associations of people, facts and objects, in a combination of efforts that involve a sociogram (rhetoric, subjectivity) and a technogram (instruments, objectivity).

Latour (1999) now turns to scientists and engineers as actors to be followed in the technological development processes, making an important digression on who should be included in this role. Thus, he demonstrates that techno science has a pure and solid "inside", which is developed inside laboratories, but has an outside, which involves public relations, political disputes, ethical problems, class struggle and lawyers.

He also demonstrates that both sides are inseparable and that the more robust the inside, the greater the distance that must be covered outside. Latour (1999, p. 258) says that *"[...] pure scientists are like helpless chicks that stay in the nest while the adults are busy building shelter and bringing food*."

Latour's aim is to demonstrate interdependence between political processes and those of nature, which he calls the “outside” and the “inside” of doing science:

> "[...] the ability to work in a laboratory with dedicated colleagues depends on the degree of success that other scientists have in obtaining resources. (...) this success depends on the number of people already convinced by scientists that the deviation through the laboratory is necessary to promote their own goals" (LATOUR, 1999, p. 259).

Thus, he broadens the role of engineers and scientists to include, in the translation model, all the people who work "outside" to enable the work of those "inside" the laboratories. In the translation model, negotiation, management, regulation, inspection, teaching, sales, repairs and communication are integral parts of the research.

Another interesting translation found by Latour is that techno science is only sustained when scientists and engineers are partners and seek convergence with the interests of other groups that are more powerful than them:

> "Scientists are only successful when they match their destiny with industry and/or when this industry matches its destiny with the State" (LATOUR, 1999, p. 279).

From this methodological rule subsume the importance that regulation, object of this research project, has for the scientific process involved in clinical research activities, highlighting not only the symmetry, but the heterogeneity of reality that is gradually built inside and outside the laboratories.

e) Latour's sixth methodological rule

> Faced with the accusation of irrationality, we do not look at the rule of logics that was broken, nor at the structure that could explain the distortion, but at the angle and direction of displacement of the observer, as well as at the extension of the network that is thus being constructed. (LATOUR, 1999, p. 422)

So far Latour (1999) has demonstrated how the interlacing of several elements that "tie" themselves to the fate of an allegation occurs, in an effort to demonstrate how controversies end, how claims become facts or artifacts or how black boxes close.

From the sixth methodological, rule Latour (1998) introduces a new aspect by stating that the production of facts and artifacts does not occur anywhere or at any time. He refers to techno science as a process of constitution of scientific facts composed of networks, whose enterprise multiplies the number of allies in a constant and sacrificial effort to keep them (LATOUR, 1999).

In the sense used by Latour (1999), networks means that the resources are concentrated in few places (such as knots) and interconnected (as if they were wires and meshes) at the same time. Through this notion of network, Latour aims to explain why the number of people who

seem to dominate techno science is limited or what roles the rest of humanity plays in dealing with the “reality” produced by translations.

The issues faced by Latour concern the judgments of rationality and the issue of relativity (LATOUR, 1999).

Latour (1999) confronts the role of the scientist in relation to the role of “outsiders”, with the analogous idea of objective-knowledge versus subjective-beliefs.

First, Latour (1999) infers that the substantiated opinion of a small group of well-positioned scientists on a given subject should prevail over the unsupported opinion of millions of people who know nothing about that subject.

On the other hand, Latour (1999) argues that the survival of beliefs, instead of knowledge, shows that the process of reality construction, considering the multitude of people involved in it, is not based solely on the criterion of rationality, but is carried by external elements that need to be considered (LATOUR, 1999).

Therefore, there would be an asymmetry between the behavior of scientists, representing a minority, and that of non-scientists, representing the majority, which end up by interfering in the process of resolving disputes, with reflections on reality.

Latour (1999) relates forces, ironically designated as “social” and “cultural”, to justify what he calls a stubborn attachment to obsolete prejudices, whose presence represents the denial of the very construction of science.

It seems that Latour (1999) recognizes a limiting factor to the closure of controversies when not guided by rationality actors choose cultural or behavioral forces as a determining criterion to see reality. This issue seems relevant because if the scientist is expected to make a judgment based on rationality, the vast majority of people judge reality based on axioms that they are not willing to question, which would contaminate the translation with irrationality.

Latour (1999) strives to understand and demonstrate what makes irrational claims persistent, and therefore he invokes David Bloor's (1991) concept of “asymmetrical explanation”.

Whilst the explanation of rational facts will depend only on a sane mind and a perfect method, irrational statements are the result of the imprisonment of “social”, “cultural” and “psychological” factors, which according to Latour’s view, do not substantively exist.

Thus, in order to reverse the result of irrationality judgments or the asymmetry of irrational explanation (BLOOR, 1991), Latour transposes the effort to a jury court where an "irrationality judgment" would occur (LATOUR, 1999, p. 304). The irrational accusers should

be asked what their evidence is, who their witnesses are, how the jury is chosen, what kind of evidence is considered legitimate, and so on.

Latour (1999, p. 311) also proposes some measures to reverse the results of a judgment of irrationality:

a) tell another story built around the same structure, but that applies to the society of who told the story;

b) retell the same story, but bringing out the context whenever there seems to be a gap in reasoning and show what kind of little-known subject the reasoning applies to;

c) retell the same story, but framing it in a different way, allowing it to go on;

d) tell another story in which the rules of logic are also violated with the detail that this story should not be about beliefs, but about the knowledge of the person who told the story.

After overcoming the efforts made by Latour to combat irrationality judgments, it seems that he surrenders to the perception that irrationality cannot be fully fought, being thus necessary to live with it:

> "Instead of living in a world made up of dotted lines, which people rarely follow, and crooked paths they often tread because they are carried by prejudices and passions, we live in a sufficiently logical world. Each one takes care of their affairs and goes on..." (LATOUR, 1999, 319)

Latour (1999) then appeals to "mitigating circumstances" of the irrationality judgment to claim another way to deal with irrationality: relativity. Relativity makes reality only apparent, which ends up by making the "asymmetry of contents" a "symmetry of forms". Thus, there would be possible coexistence between people who live in different worlds, or who have different beliefs, making relative the controversy and enabling its closure by reflex:

> "[...] now we have changed: from debates about reason, we go to disputes around what the world of different people is made of, how they can achieve their goals, what stands in their way, the resources that they can be sought out to open the paths for them. [...] how can the statements that contradict it be unraveled? No one is accusing anyone of irrationality, but we are still struggling to live in different worlds" (LATOUR, 1999, p. 324).

The relativity defended by Latour leads him to recognize that people do not live immersed in "cultures", do not belong to "societies", nor do they live under "paradigms" without colliding with each other. What matters then would be the mapping of these differences among what Latour will call "chains of associations" (LATOUR, 1999, p. 330).

People strive to make their claims more acceptable than those of others, and do so through unpredictable and heterogeneous associations or translations, taken to a growing intensity of controversy. In order to decipher them, it will be necessary to understand (LATOUR, 1999, p. 331): (a) how the attribution of causes and effects is made; (b) which points are interconnected;

(c) what dimensions and what strength these connections have; (d) who the most legitimate spokespersons are; and (e) how all these elements are modified during the dispute.

The main challenge of mapping these associations between things, words, customs and people is not to make any additional assumptions about their reality. In this effort, accusations of irrationality would be removed by accepting the relativity in which they are immersed, leaving us to observe the angle, direction and movement of the associations that are carried out. (LATOUR, 1999).

In the end, Latour (1999, p. 336) shows that he is not interesting in finding out whether people are right or wrong about their assertions, but in the “socio-logical” paths they take, how many people they take with them and what kind of vehicle and facilities are provided for this trip.

Non-attacked statements are assumed as objective, but when someone “crosses the path” of another person, it is necessary to understand the dynamics of these movements between the inside and the outside of the networks.

Latour presents what he calls the "fact makers' paradox", which is:

> “at the same time, increase the number of people who participate in the action – so that their claim spreads – and decrease the number of people who take part in the action – so that it spreads as it is” (LATOUR, 1999, p. 339).

The paradox was solved by the translations of interests and by the automation consistent in the connection of humans to artifacts and objectives for the production of hybrids, giving thus the characteristics of technoscience.

However, in translations in which a margin for negotiation is left so that each actor adapts the statements to local circumstances and interests, the statement will become "softer" and unable to break habits or behavior patterns, and this is the behavior of statements that circulates outside the networks of controversy. This is the case, for example, of popular sayings, which are adjusted, incorporated, negotiated, adopted and adapted without major conflicts between people (LATOUR, 1999).

On the other hand, among scientists and engineers it is customary to increase control and reduce the margin of negotiation over the statements, causing many resources to be enlisted so that they become "hard facts", although less people will be interested in that proposition (LATOUR, 1999).

Thus, Latour (1999) points out that “harder” facts are not naturally better than “softer” ones, which implies that the paradox of fact-builders may be solved in two opposite ways: one that extends wide networks and another that closes them.

Hard facts are rare and costly occurrences. Soft facts are more frequent and less conflicting occurrences. On the other hand, there is a direct relation between the number of people one wishes to convince, the angle at which an allegation collides with others and the hardening of the facts (LATOUR, 1999).

f) Latour's seventh methodological rule

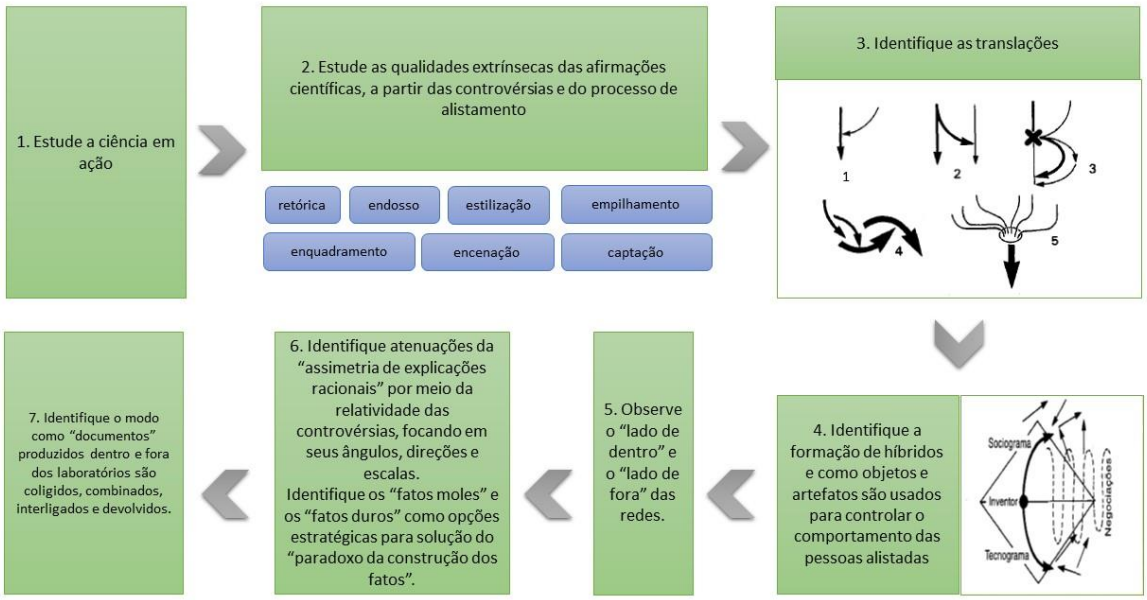
> Rule 7. Before attributing any special quality to people's minds or methods, let us examine the many ways in which entries are collected, matched, linked, and returned. Only if something goes unexplained after studying the network should we start talking about cognitive factors. (LATOUR, 1999, p. 422).

In this methodological rule, Latour (1999) explores the idea of movement on the production of knowledge in a network. He refers to movement as closeness and detachment regarding work in the “inside world” and the “outside world” of the “laboratories”. He emphasizes the result of these movements by focusing on recording documents that are combined in different ways in this dialogue of work between scientists from “inside” and scientists from “outside” the laboratories.

Due to this displacement, which generates data and evidence, the representations of reality generated by such evidence are essential, and Latour will refer to them as information or forms. Without them, translations between humans and non-humans would not be possible, and therefore, it is necessary to understand how this documentation is produced in this movement of displacement implicit in technoscience.

A summary of the seven methodological rules can be found in the figure below:

Figure 9 Latour's methodological rules



Source: Latour (1999), adapted by the author.

3.2 Sources of Latour's Uncertainty

Besides the methodological rules for the construction of scientific facts (LATOUR, 1999), in his work Reassembling the Social (2007), Latour (2007) refers to the construction of the social in procedural terms, raising five sources of uncertainty that permeate the process of constructing reality, and should be faced in the methodological path upon the following recommendations.

a) The first source of Latour's uncertainty

> There are no fixed groups and actors must be followed in order to trace connections. The formation of groups and anti-groups is done by the actors. The actors are able to define their social context and compose their set of associations. Objects are kept as mediators for as long as possible.

Latour (2007) does not deny the existence of groups, but only their substantive nature. It is in this sense that he claims that there are no groups, but only groups in formation. This does not prevent groups in their procedural nature from being considered macro-actors or institutional actors, reified or in their state of punctuality, without missing the point that they are also in flux, with their actors-networks associating by controversies and translations while

the social aggregates, disaggregates and reassembles as if in a constant way. Latour (2007) deals with uncertainty about groups, as follows:

First, to outline a group, one must look for those who speak for the group. Second, to recognize the boundaries of a group, one must look for what or who the anti-groups are. Third, when groups are formed or redistributed, their spokespersons will always find ways to define and preserve them, based on tradition or law. Fourth, social scientists are also called to participate in the sustainable definition of groups.

Organization takes place in a performative way, where the group has to be explained and maintained by the several ways that enables its existence, unlike an ostensible view, in which the group is seen as a finished and naturally stable definition (LATOUR, 2007).

Latour (2007) also presents the differences between mediation and intermediation. While intermediaries carry meaning or force without transforming the nature of reality, mediators "transform, translate, distort and modify the meaning or the elements they supposedly convey" (p. 65).

Thus, aggregation and maintenance of groups occur through translational processes driven by controversies managed by a few actants who act as mediators among a countless number of intermediaries also active in institutional dynamics.

Therefore, from this uncertainty comes the lesson that it is not advisable for the researcher to define the basic element of what the world is made of (LATOUR, 2007) before the actors do so, and in their place.

b) The second source of Latour's uncertainty

> The action is not conscious, but it is articulated, and this is what the researcher must describe. It is not the context that pushes it and it does not occur from the individual alone. Controversy mapping. Identification of actants

The second source of uncertainty concerns the heterogeneous nature of the ingredients that form social bonds. This shows that the action does not occur under the full control of consciousness, but derives from a conglomerate of actants in a dynamic state of aggregation, and surrounded by movements of coalitions, controversies and translations.

The idea of the actor is neither personified nor identified, and it is assumed that it is never clear who or what is acting in the institutional dynamics. For this reason, the recommendation is that "any interview, narrative or comment, however trivial it may seem, will enrich the analyst with an astonishing set of entities to apply the course of an action" (LATOUR, 2007, p. 77).

Latour (2007) presents a list of characteristics that are always present in contradictory arguments about what happens in social dynamics.

a) Actions are part of an account as responsible for a feat, as something that affects a state of affairs. Thus, without reporting a significant argument capable of generating transformation one cannot talk about an action. Therefore, it will always be necessary that reports on actions bring evidence regarding what observable traits can be found about them.

b) Actions are not to be mistaken with their figurations, which constitute different items from the researcher's list. Therefore, the word actant replaces the notion of actors, and this is also the reason why ANT adopts narrative theories, considering its freedom of movement and inventive possibilities. According to Latour (2007), the idea is “to register, not filter; describe, not discipline” (p. 87).

c) Actions oppose other rival actions, just as groups need the identification of anti-groups for their outline.

Latour's (2007) final recommendation is not to choose one figuration among many to replace actors, but to increase in the reports the proportion between mediators and intermediaries so that the abundant action generates the concreteness of the social dynamic.

c) The third source of Latour’s uncertainty

> Objects are endowed with agency, and there is a need to describe their roles in action and in tracking social connections

From the notion of non-intentionality in human actions and from the performative option of the ANT approach, full of symbolism and reflexivity, one draws the conclusion that it is possible that objects also act on reality (LATOUR, 2007).

Latour demonstrates that you cannot drive a nail without a hammer, nor boil water without a pan. Therefore, even if there is no intentionality, objects participate inexorably in the aggregation of the social. However, things can also "authorize, allow, grant, encourage, trigger, suggest, influence, interrupt, enable, prohibit etc." (LATOUR, 2007, p. 109).

In order to the agency of objects to be perceived, two contradictory requirements must be met in ANT: on the one hand, the sociologist must not be limited to social ties, and on the other hand, the researcher must not become a specialized technician.

Among the recommendations made by Latour to solve the uncertainty regarding the participation of objects in the aggregation of the social, we highlight the following:

a) Innovations must be studied at the artisan's workshop, at the engineer's design department or at the consumer's home, places in which "objects live a multiple and complex life, through meetings, projects, sketches, regulations and tests" (LATOUR, 2007, p. 120).
b) The mediation of objects can be noticed when the problem of distancing in time, space and capacity is solved. Therefore, even strange, exotic, archaic or mysterious implements must be considered. This issue becomes particularly relevant because it justifies and endorses the choice we made in this project of rescuing the different meanings of regulation, deriving from homeostasis, going through thermodynamics, until reaching the human sciences such as Economics and Law. Or else, when we discuss the very notion of health from ancient, medieval, modern times, until we reach health systems that were also linked to a health industry, represented by the pharmaceutical sector, until we reached clinical research. Bringing these elements into the work is supported by Latour (2007).
c) Even silent intermediate objects can become mediators, such as the one we have been experiencing due to a virus that suddenly affected humanity, imposing on us severe restrictions and changes in the behavior of governments, companies, people and even other objects.
d) Objects that go backstage can be brought back through files, documents, souvenirs, museum collections, and will serve to produce “the state of crisis in which machines, resources and implements were born” (LATOUR, 2007, p. 119).

d) The fourth source of Latour’s uncertainty

> The “construction” of the fact that focuses on the scene in which human and non-human beings merge is supported by social constructivism. The social scientist's job consists of generating hard recalcitrant facts and passionate objects that resist to social explanations.

In his fourth source of uncertainty, Latour (2007) seems to turn to the scientific aspect of the social. The suffix "-logy" in the word "socio-logy" is questioned. This is because Latour raises an epistemological question about the plausibility that facts are actually constructed without subverting the procedural logic that the aggregation of the social is a constant movement. In other words, this work does not stop and that is why there is not a true construction.

The discussion proposed by Latour (2007) involves a movement that starts from metaphysics and reaches ontology regarding the understanding of what really constitutes the real world.

From a metaphysical point of view, reality could easily be taken for representations, whilst from an ontological point of view reality needs to be composed empirically. Thus a list of recommendations is formulated by Latour (2007):

a) Consider that scientific facts are not discovered, but manufactured in different ways and in different places;

b) The manufacturing locations of scientific facts are not limited to laboratories, but are also easily traceable.

c) The experiments and controversies generated by the facts provide a kind of "continuous site" that offers a continuous source of information capable of generating changing ontologies of social reality.

e) The fifth source of Latour's uncertainty

> Bring to the foreground the very act of composing reports with the aim of weaving a network, recording differences, absorbing multiplicity, being restructured in each case. It takes on a reflective, articulate and idiosyncratic role in the production of accurate, faithful, interesting and objective texts.

Finally, Latour's (2007) fifth source of uncertainty refers to the so-called risk reports, which consist of types of studies carried out under the label of social science, but which contain the very act of writing reports.

As in a social scientist's laboratory, Latour (2007) states that the task requires skill and writing skills to describe in an objective way the connections present in the investigated phenomenon. Latour (2007) claims that the aim is not only to write a story, but a true and complete report on the topic that one intends to study.

Latour (2007, p. 189) states what he considers to be a good text: (a) it is the one that "weaves a network", (b) in which "each participant is treated as a complete mediator"; (c) a narrative in which "all actors do something"; (d) where "each point in the text can become a crossroads, an event or the origin of a new translation".

Then, in order not to miss the movements to be studied, Latour (2007) suggests that different notebooks are used, as listed below:

a) first notebook: consisting of the research diary itself;

b) second notebook: for recording the items in chronological order and framing into categories for transformation into files and sub-files;

c) third notebook: for drawing up drawings and sketches;

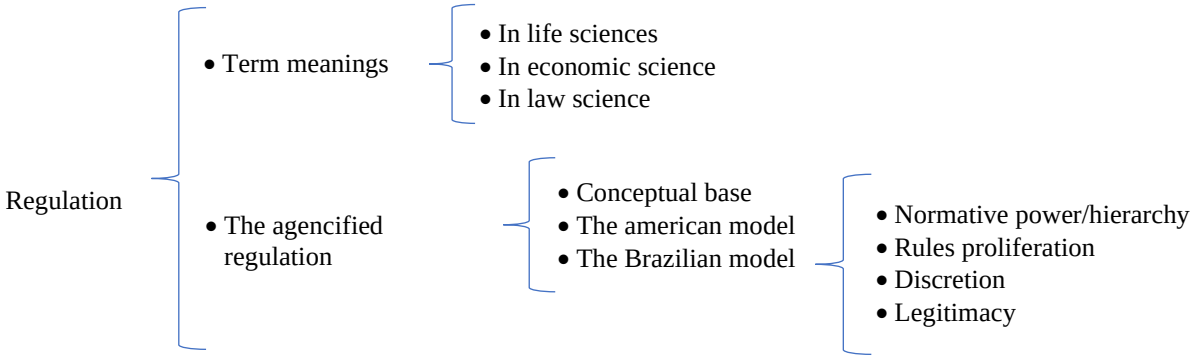
d) fourth notebook: to record the effects of the written report on actors whose world has been unfolded or codified.

4 REGULATION

This section ranges several approaches to the term “regulation” and then focuses on the concept of “agencified regulation”, dealt with by legal theory. We chose a conceptual retrospective, which explains the phenomenon of agencification from the North American experience, and how this model was imported into the Brazilian experience.

Further, issues related to the normative authority of Brazilian regulatory agencies will be addressed, emphasizing: (a) the problem of coexistence between rules from regulatory bodies and law in strict sense; (b) the issue of proliferation of regulatory standards in the legal system; (c) the issue of discretion granted to regulatory authorities for the exercise of their functions and (d) the legitimacy and popular participation in the regulatory activity.

Figure 10 Development of the chapter on regulation



Source: The actor

4.1 Meanings of the term

There are several meanings for the word 'regulation' and some of them prove to be useful for the approach of ANT because of its heterogeneous characteristic, and since it is an actant to be considered in the research.

Regulation has been present in several areas of knowledge and has been associated with the divine (theology), homeostasis (biology), control (mechanics), power (political science) and normativity (sociology and law).

According to Canguilhem (1977), it was the German philosopher and mathematician Gottfried Leibniz who, in the 18th century, offered the bases that most influenced modern

conceptions of regulation, attributing to God the role of preserving what he called “initial constants”.

This first notion strongly influenced physiology, economics and politics, as it attributed to regulation the same divine role of conservation, restoration of closed systems and/or maintenance of balanced environments.

The epistemological fragility of regulation (PRÉVOST, 2000) and its consequent heterogeneity justifies a rapid incursion of its conceptual possibilities in the various areas of knowledge that have traditionally used it.

In a biological sense, Canguilhem (1977) points out that physiologists adopted the term in a metaphorical sense to explore the regulatory functions of the animal organism.

Biological regulation supposed the conception of a living being as a system, whose mechanisms are located in a relation of interdependence. Among the main ideas, the following stand out: (a) the interaction relations between several parameters that are foreign to each other, (b) the identification function of an effect, (c) the detection function of a deviation or difference in relation to a given reference point, and (d) the correction function of an effect (RUMELHARD, 1994).

From the 19th century onwards, the notion of regulation evolved to also meet the need to seek a dynamic balance aimed at improving systems of transformation.

Prévost (2000) reports that the concepts of biological regulation were exported to physics, contributing to the development of the cybernetic theory, which is based on feedback relations and, thus the association of regulation with the notion of conservation or restitution has been expanded to become a function of compensation and adaptation (CANGUILHERM, 1977).

Piaget (1977) observed that the possibility of achieving a dynamic balance whereby opposing physical forces would become self-organizing was crucial to the development of a “regulatory” epistemology. It would then be possible to conceive of the possibility that changing systems would be capable of reinventing themselves.

With this, the idea of regulation crossed different scientific disciplines, ranging from biology and thermodynamics, then cognitive sciences such as politics, economics, sociology and law.

In the spectrum of economic sciences, 'regulation' is conceived as a strictly formal set of any normative prescriptions that discipline individual actions and social interactions, whose role is the formal control of a productive activity carried out by a state authority.

These rules seek to rule activities such as finance, transports, education, health, communications and even the operation of the labor market.

The study of regulation in economic sciences is developed from different perspectives, but in all of them regulation is presented as a mechanism for containing or controlling “market failures” or “State failures”.

There are different approaches to the subject, which can be divided into at least four groups, each aimed at answering different questions related to the regulation of economic activity.

First, the Marxist-influenced School of Regulatory Economics considers regulation as an imperative response to so-called “market failures”. The regulatory agent would be concerned only with the allocation of resources with the ultimate objective of maximizing social welfare (MYLES, 1995).

Second, the School of Political Economics of Regulation, which denies that the regulatory authority is indifferent to groups of pressure or interest and reaffirms the political power of such agents as present in the regulatory activity. Therefore, the State would be seen as an entity comprising persuadable individuals. For this reason, regulation would be seen as a market object (STIGLER, 1971).

On the one hand, politicians and bureaucrats, endowed with personal interests and aspirations, seek to be re-elected to maintain their political-administrative functions to ascend the state hierarchy and even to increase their income expectations. On the other hand, companies are looking for regulations to protect themselves from competition, create tax breaks, obtain subsidies and to gain greater control over competitive market forces.

This school sees regulation as a process to respond to the objectives of interest groups; the excessive costs of regulation are also highlighted. Faced with its complete distortion, its theorists generally conclude that the solution would be the simple suppression of regulation, given its distortion or uselessness (STIGLER; FRIEDLAND, 1962).

Third, there is the School of the New Public Economics of Regulation, represented by Jean-Jacques Laffont (1982), which seeks to characterize the faults of the regulator and regulatory provisions to correct them or minimize their perverse effects.

According to Laffont (1982), regulatory faults would be identified by (a) information asymmetry between regulatory agents and regulated entities; (b) personal interest of the regulator; and (c) faults associated with the regulator's insufficiency of credibility.

Last, there is the institutional economics of regulation, represented by the New Institutional Economics theorists. North (1990) defends that there is no a priori mode of coordination of productive activity more effective than another, and that the effectiveness of

different alternatives of institutional arrangements should be evaluated by a comparative criterion of costs and benefits.

Thus, the criterion for measuring the presence (or not) and the level of regulation will depend on the structure that rationalizes the lowest possible transaction cost. In other words, the origin of regulation would be found in transaction costs, but it is possible that regulation itself causes even higher transaction costs, and it is therefore necessary to examine vis-à-vis a governance structure that maximizes efficiency, which may even lead to a laissez-faire situation in economic activity.

In the field of legal sciences, regulation is developed under two aspects: (a) the first one has an etymological focus and refers to the establishment of rules and standards aimed at controlling social behavior; (b) the second one is influenced by the biological concept and sees regulation as a means of maintaining or restoring the balanced functioning of a system.

Integrating both aspects, in a broad sense regulation would consist in ensuring the balance required by law between the rights and obligations of each individual.

In a restricted sense, regulation is the creation of state legal standards that will discipline the exercise of certain activities, predominantly those of economic nature, in the face of the presupposed denial of self-regulation by the invisible hand of the market.

It is important to emphasize that in the Brazilian legal area the word 'regulation' was adopted since the State reform movement took place in the early 1990s, especially as a result of the privatization of state-owned companies and the maintenance of the idea of competition between concessionaires in the provision of public services (GUERRA, 2015).

Upon the privatization process it was deemed necessary to create a mechanism that would maintain a portion of control over the economic activities that were handed over to the private sector.

Therefore, the concept of regulation in Brazilian law represents a set of formal or dogmatic legal norms that act within the scope of the State's attributions and its intervention in the economic domain (DI PIETRO, 2004).

Although the concept of regulation can be applied to any social object, in the legal field it has been used particularly within the scope of the standards that regulate the participation of the State as an economic actor and in the subsequent process of decentralization of public services.

Thus, the discussion that follows in the legal field regards the so-called process of privatization of economic activity, by which the State would abdicate its direct action as an

economic agent, but would create mechanisms to maintain control over activities transferred to the private sector.

This new role of the State would be present in different levels of deconcentration and decentralization (ranging from models of mere grant, permission and concession to pure privatization) and would alter the correlation of forces between the so-called state powers, embodied in the theory of separation of powers, which conceives the State under three autonomous but interdependent powers: the legislative power, the executive power and the judiciary power.

Then, in the field of law, an institutional innovation emerged on the regulatory modus operandi: it would no longer be the powers of the State, represented by the executive, legislative and judicial bodies that would operationalize the regulatory activity, but a fourth entity of a special autarchic nature with a collegiate decision-making process, fixed terms and in staggered terms for its directors, administrative and decision-making autonomy, bringing together executive, regulatory and judicial functions (GUERRA, 2015).

Therefore, the so-called "Regulatory Agencies" were introduced into the bureaucratic structure of modern States.

4.2 Agencification of regulation and its variations

In this section, we will focus on the process that describes the emergence and evolution of "regulatory agencies", which for the purposes of this research project will be considered as one of the actors in the institutional dynamics to be scrutinized.

a) The theory of separation of powers as a starting point to understand the regulatory agencies

The regulatory power, exercised through a "state agency", stems from the understanding, evolution and even a relative softening of the well-known theory of separation of state powers, which precedes the very notion of regulation.

The first notions of a subdivision of the State were attributed to Aristotle who, in his work "The Politics", glimpsed the existence of three distinctive functions, which although distinct were performed by a single sovereign power: the function of editing general norms, the function of applying them to the concrete case and the function of settling conflicts arising from the execution of the general rules in concrete cases (LENZA, 2018).

According to Aristotle, these functions would be concentrated in the hands of a single person, but in modern times these powers would be exercised by distinct, autonomous and interdependent bodies.

This change was the result of a long evolutionary process that began in England and spread throughout the West. This is explained due to the fact that the “Glorious Revolution” consecrated the “Bill of Rights” in 1689, from which both the royal authority and the authority of the parliament were equally placed, thus laying the first bases for an organic, not just functional, separation between the powers that had been identified by Aristotle.

This new organic division of powers was systematized and widely reflected in the work of the Frenchman, Baron de Montesquieu, entitled “The Spirit of Laws” (FERREIRA FILHO, 2008), representing a milestone for the organization of governments in modern liberal states.

According to the classic and modern conception of the separation of powers, the Legislative Power is responsible for creating laws that will discipline, regulate or control social life. The Executive Power is responsible for the concrete acts of decision-making, power and, ultimately, enforcement of the laws that constitute the legal system created by the Legislative Power. Finally, the Judiciary Power is a moderating power, which holds the monopoly of the Jurisdiction, which consists in the activity of interpreting the law and applying it in situations of conflicts of interest between the jurisdictions, including the State itself, personified by its three powers.

In its modern sense, the foundation of the separation of powers would be based on the idea of protecting individual freedom so that the division of power would impose on the rulers the need for collaboration and consensus in decision-making. On the other hand, mechanisms of inspection and reciprocal responsibility between state powers would be established, which was enshrined in the North-American law as the system of "check and balances" (GAD, 2010).

Slowly, the theory of separation of powers is being adopted by most modern States, and gradually an interpenetration between the powers or the attenuation of the classical theory that defended a pure and absolute separation between them is being accepted.

Thus, in addition to exercising typical functions inherent to each of the three State bodies, they could atypically exercise the functions of each other. In other words, the Legislative Power, which is given a typical legislative function, would atypically exercise executive and judicial functions. The Executive Power was also assigned legislative and judicial functions. Likewise, the Judiciary Power was given atypical functions of legislative and executive nature.

However, it was under the US law, in the scope of issues regarding State intervention in the economic field, that the model of separation of powers, although already attenuated, gave

in even more to admit a new actor in the institutional framework of that country: the regulatory agencies.

b) The North American agencification model as a first manifestation of the new regulatory law

The regulatory agencification model, which began in Brazil in the 1990s, is not unprecedented, but reproduces in part the North American experience that began in the mid-19th century, starting from the regulation of steamboat transport (Steamboat Inspectors) and the interstate rail system (Interstate Commerce Commission) (GUERRA, 2015).

Thus, we believe that a brief contact with the North American experience will help to understand what happened in the Brazilian regulatory process.

The United States of America was founded with the notion of the tripartite separation of powers and with the view that the powers held by the Executive Branch, in the person of its president, would be specific, vaguely explained in the constitutional text, relatively limited and immune to any form of will, possibly as an effect of the repulsion to the tyranny that the North Americans had suffered by their colonizers (GUERRA, 2015).

As a second trait of the North American state organization, the separation would not be absolute, but mediated in a balanced way that sought to prevent any of the powers from standing out in relation to the other. Thus, the lack of details of the American constitutional standard brought some flexibility to the interpretation of its provisions.

Given to the fast industrialization process, which culminated with the emergence of trusts, cartels, concentration of wealth, corruption in the state machine and several social problems, there was a need to increase the efficiency of the activities of the State, which took place through the bureaucracy expansion under a new regime called “administrative state”, also represented by the expressions “bureaucratic state”, “capitalist state”, “corporate state”, “postindustrial state”, “regulatory state” and “welfare state” (SKOWRONEK, 1982).

The Americans recognized the limitations of the classic tripartite exercise of state power to deal with complex modern problems, and began to increase the state structure with the creation of commissions, or sector agencies, composed of technical staff and endowed with functions similar to those of the executive, normative and court from the powers of the State (MCCRAW, 1984).

The emergence of American agencies happened along with several important events in the beginning of the 20th century.

The following stand out: a) the "Square Deal", which was a program developed from 1906 onwards by the then president Theodore Roosevelt, whose emphasis was on combating plutocracy through the creation of numerous antitrust laws, in addition to mechanisms to regulate social issues, labor, health (medicine and food), health inspection, education, rural areas and natural resources; and b) the “Great Depression” of the 1930s, which triggered the “New Deal” program, created during the government of President Franklin Roosevelt, by which the Executive Branch and the Congress would restructure the state machine to fight the huge economic and social problems that the country was facing.

Thus, American agencies emerged as a reaction to the need to adapt state functions to the new reality arising from industrialization and its effects on the US economic and social life. Their trait was the fact that they had been created by the National Congress as governmental entities with authority to direct and supervise the implementation of certain objectives approved by law, such as monitoring complex matters of government concern, disciplining daily issues or managing crises.

The activities of the agencies were not supposed to be confused with the three established powers, and a new state function was being recognized; it was called “administrative” or “regulatory”, and it was distinct from the legislative, executive or judicial functions (GUERRA, 2015).

They would be created by law and supervised by the elected authorities, that is, the Congress and the President of the Republic, in addition to counting on the participation of society (rule-making process), which would give legitimacy to their decisions (GUERRA, 2015) .

In the US, agencies fall into three categories: executive agencies (independent or otherwise), corporations, and regulatory agencies.

Executive agencies operate under the supervision of the executive branch, and it is important to point out that if their officers cannot be unfairly dismissed by the President of the United States, this means that they are independent. On the contrary, when their directors are dismissed ad nutum, they are mere extensions of the Executive Power, analogous to state bodies connected to the direct public administration of the Brazilian system.

In the US, most independent agencies have a legal provision in the sense that their leaders necessarily belong to the two main political parties (the two-party system), which prevents vacancies from being filled only by members of the presidential party. Furthermore, the tenures are in most cases not the same as those of the President; finally, the nominations of directors are submitted to the Senate (GUERRA, 2015).

Corporations, or government corporations, are agencies that in fact operate as companies, since they produce goods and provide services, and are equivalent to Brazilian legal entities of indirect administration, such as mixed capital companies and public companies.

The third type of agency in the North American model is that of regulatory agencies, which are mostly linked to the Executive Branch and are characterized by the prerogative of the so-called exercise of police power that comprises the functions of inspecting, supervising, controlling and, above all, punishing acts contrary to the field of regulation.

The evolution of the North-American regulatory system can be divided into several phases. Maccray (1984) and Deleo (2008) categorize them as follows: a) 1837 to 1887: phase characterized by the regulation of trade by state governments; b) 1887 to 1906: period between the Agrarian Reform and the creation of the Interstate Commerce Commission (ICC); c) 1906 to 1917: period known as the progressive phase; d) 1920 to 1929: influence by the post-war period; e) the 1930s: characterized by the reorganization of economic activity as a result of the 1929 depression; f) the 1940s: characterized by mobilization for war and national defense, with emphasis on the creation of the Administrative Procedure Act (1946), which provided a strong proceduralization of regulation; g) the 1960s: known as "social regulation", characterized by emphasis on fighting discrimination, consumer fraud, health, safety and environmental protection; h) the 1970s: known as the "rulemaking era" (SCALIA, 1981) due to the excessive number of highly complex and detailed regulatory rules (micro regulation); i) The end of the 1970s to the present day: characterized by criticism to regulation due to the capture of agencies by the regulated and the rise in regulation costs for society; this phase is known for its tendency towards deregulation.

c) The Brazilian model of agencified regulation

The Brazilian experience of regulation is based on the assumption that our tradition has never been liberal like the North American model, and that is the reason why the strong interventionist character of the Brazilian State may explain the fact that we have been so late in adopting the agencified regulatory model that has been used in the United States since the 19th century.

Throughout the republican period, Brazil was structured around the classic separation of powers, with a strong presence of the State in the economy, including numerous public entities responsible for controlling the production and trade of several products.

The following entities under the provisional government of Getúlio Vargas are a good example: National Institute of Sugar and Alcohol (IAA); National Coffee Department (DNC); National Institute of *Mate* Tea (INM); National Petroleum Council (CNP); National Institute of Salt (INS); Reinsurance Institute of Brazil (IRB) and National Institute of Pine (INP). In 1951 the development policy of Getúlio Vargas was resumed by creating the National Institute of Coffee (IBC) and PETROBRAS.

Under the government of Juscelino Kubitschek, the State expanded its direct action in the economic domain upon the creation of several companies such as NOVACAP, Centrais Elétricas Furnas, Rede Ferroviária Federal S/A, COSIPA and ELETROBRAS, among others.

The military period, between 1964 and 1985, continued to be characterized by the strong presence of the State in economic relations, but included the National Program for De-bureaucratization, which in 1979 began a process aimed at simplifying the operation of Public Administration.

This phase corresponded to the beginning of the political redemocratization process and also represented a signal to dismantle the Entrepreneurial State, which would only take place in 1996 with the intensification of privatizations and the creation of the first autonomous regulatory agencies, under the government of Fernando Henrique Cardoso.

Among the characteristics of the North American agency model, only two were effectively adopted in the Brazilian system: (i) a fixed term ("tenure") for the agency directors, with terms that do not coincide among the members of the collegiate; and (ii) decision-making independence regarding the Chief of the Executive Power (GUERRA, 2015).

The collegiate administration of regulatory agencies – with deliberative quorum by absolute majority – was not necessarily a novelty, since in Brazil there were direct or indirect administration bodies with these characteristics.

While Fernando Henrique Cardoso ruled the country, nine federal regulatory agencies were created in Brazil: National Agency of Water (ANA); National Agency of Civil Aviation (ANAC); National Agency of Telecommunications (ANATEL); National Agency of Cinema (ANCINE); Agency of Electric Power Agency (ANEEL); National Agency of Oil, Gas and Biofuels (ANP); National Agency of Waterway Transportation (ANTAQ); National Agency of Land Transportation (ANTT) and National Agency of Health Inspection (ANVISA).

Likewise in the USA, in Brazil there was a lot of questioning about whether the regulatory agencies were constitutional. When the Brazilian Supreme Federal Court was inquired, it was found more advisable to ratify the agencified system, validating the tenure system, the

normative functions (with reference to their secondary nature and subordinated to the law regulation) and the decision-making autonomy.

Among the sources of controversy that have given rise to a continuous improvement of the agencified model of regulation, we are interested in a thorough examination of the normative power of regulatory agencies in Brazil concerning: (a) the hierarchical position of regulatory standards within the system, (b) the problem of profusion of the regulatory norms created, (c) the discretion of regulatory acts, and (d) the issue that refers to popular participation in the regulatory activity.

It is important to deal with the normative function of regulatory agencies because it represents one of the Gordian knots of the agencified model and because it constitutes an inexhaustible source of controversies that has raised the regulation performativity.

c.1) The hierarchical position of regulatory standards in the Brazilian system

The first issue arising from the regulatory normative power concerns the positioning of the rules produced by the agencies in relation to the laws produced by the Legislative Power in the strict sense.

There is a consensus that there is a hierarchy between laws in the strict sense and regulatory rules, which, at first could denote the sense of limiting the reach of the normative power of the regulatory agencies as a dependence function and their conformation to formal laws .

According to Medauar (1999), the difference between normative power and regulatory power lies in the fact that the former comprises the production of autonomous standards, while the regulation is intended to establish open and ordering conducts of administrative action, so as to clarify the application and execution of laws aimed at Public Administration.

Carvalho Filho (2008) also points out the distinction between the words “regulatory” and “regulate”. The first means to complement, specify and always supposes that there is a higher hierarchy rule susceptible to this complementation. The notion of “regulate” involves disciplining, regulating and does not require that its objective complements another norm.

In this case, the Regulatory Agencies would exercise a regulatory function, which includes the discipline of legal provisions, observing the complementarity under parameters controlled by the law that delegated the regulation to the Agencies.

Barroso (2001) called this function as a kind of “delegation with standards”, through which the Legislative Power would be responsible for establishing regulatory acts.

However, there is still the issue regarding how to ensure that the aforementioned parameters established by law are respected by the regulatory authorities, and thus consider that the standards produced achieve the objectives of the law. Carvalho Filho (2008) points out some of these parameters.

The first one refers to the choice of people who have regulatory authority, thus inferring that the appointment of directors not linked to political activities in the strict sense would be an indicator that the regulatory normative power is exercised without injunctions of interest to politics or political parties.

The second parameter is efficiency, which would be measured by the recognized competence of administrators in performing their functions. If the assumption of the agencified model is complexity and specialty of the new normative demands, then it is to be expected that the new model will be led by administrators who are fond of the sector and have recognized technical competence.

A more realistic explanation for the definition of parameters for the elaboration of regulatory norms lies in the distinction established by Robert Alexy's Theory of Legal Argumentation, which subdivides norms into two types: “standards” and “rules”. In the first group would be the “optimization commands”, the guiding principles, the general beacons of the system, while in the second group would be the specific rules for day-to-day and concrete situations.

Thus, while formal laws in the strict sense would represent standards, regulatory norms materialize rules, specifying and detailing concrete situations.

It so happens that the prevalence of this new structure of legal norms, which subdivide them into principles and rules, entails a more relaxed view of hierarchy between norms, providing greater flexibility for the elaboration of regulatory rules.

Therefore, the understanding of a rigid hierarchy has been replacing a normative structure by which laws establish principle rules, recommendation or standards, and regulatory agencies are given the possibility of creating specific and detailed rules for all situations deemed necessary for the regulatory authority's control according to legal principles.

c.2) The profusion of regulatory standards

A second issue, which arises from the previous one, and that has been denounced for generating adverse effects on activities subject to regulation, concerns the profusion or proliferation of regulatory normative acts created by the agencies.

Under the pretext of seeking efficiency and expertise in disciplining complex issues that the Legislative Power would not be able to regulate, Brazilian regulatory agencies have produced a wide range of regulatory standards.

For some, this abundant normative production reflects exactly the desirable reaction of achieving an accelerated pace in decision-making processes, characteristic which justifies the existence of these agencies.

However, others consider that this normative profusion has been received as excessive to the point of making it difficult to follow hundreds (if not thousands) of rules, in addition to those that come from the Legislative Power, making regulatory law even more distant from the people who are affected by them. .

c.3) Discretionary nature of regulatory acts

The third issue arising from the regulatory power is more comprehensive to reach any decision-making process under the competence of regulatory authorities. I refer to the problem of how decision-making autonomy is developed within the scope of activities performed by agencies, through what is called “discretionary power”.

Glauco Guerra (2016, p. 31) defines discretion as “the faculty of the public administrator to guide the administrative act according to opportunity and convenience, creating a 'free space' between the public interest and the choice of material and formal means of its realization”, although it is a consensus that the discretionary will can never be completely detached from the law, under penalty of becoming an arbitrary act, therefore not protected by law.

Different modalities of discretion are recognized, based on the classification of Miguel Sánchez Moron, cited by Volotão (2015), among which we are interested in highlighting regulatory discretion, technical discretion and administrative discretion.

Regulatory discretion occurs in cases where a regulation has been issued to execute or clarify a law, as is typically the case in the context of the normative power of regulatory agencies.

Technical discretion takes place in cases where law grants a margin of appreciation for decision, aiming at results based on evaluations that are only technical. In this area, non-determined legal concepts are frequently used, thus reducing the scope of legal control on administrative acts provided by this kind of discretion.

Management or administrative discretion corresponds to the possibility of taking individual, specific and day-to-day decisions in the regular performance of their duties,

considering the absence, excessive abstraction or imprecision of laws or normative acts in general.

Regarding the level of discretion to be examined in the activity of regulatory agencies, we must contrast several elements that act together in the process.

On the one hand, one of the pillars of the agencified regulation model resides precisely in the independence or decision-making autonomy of the authorities invested with this power and free from political interference.

On the other hand, rules and regulatory decisions are controlled by a normative power that establishes limits and criteria arising from ordinary laws that delegated the regulatory function to them, with complementary and special characteristics, under penalty of legal invalidation of rules or regulatory decisions in case of disrespect.

It turns out that the notion of "standards" or non-determined legal concepts present in the laws that delegate competence to the Agencies gives them greater flexibility and autonomy, which means that the regulatory authorities would be able to act at their discretion, according to convenience and opportunity.

In fact, upon a structure that combines autonomy and control, rigidity and flexibility, it is unclear what reflexes the relativization of legislative delegation and the profusion of regulatory norms have generated on the levels of discretion of the activities performed by regulatory agencies.

c.4) Legitimacy and popular participation in regulatory agencies

Lessa Mattos (2011) points out the relevance of the problem when introducing the issue regarding legitimacy of the normative and decision-making power of regulatory agencies which, without stricter procedural parameters that limit their regulatory, technical and management discretionary powers end up by transforming the normative and decision-making process into something dominated by arbitrary power and with no legal control.

According to the author, if the control of discretionary administrative acts is not strong enough upon the fact that judgments of convenience and opportunity (or the so-called administrative merit) would not be subject to judicial control, or in case there is only a formal control over the legality of regulatory rules, there is a risk of loss of legitimacy over the regulatory normative power. Furthermore, it seems that this view converges with the criticism of the School of the New Public Economy of Regulation, represented by Jean-Jacques Laffont (1982).

The issue regarding the potential distortion of the discretionary regulatory process to recognize arbitrary practices and the consequent loss of legitimacy of regulatory agencies raises a final question, which is to verify in what terms this legitimacy could be reinforced through a participatory democracy in the normative and decision-making instances of the agencification model.

The issue is complex, and according to Justen Filho (2011), requires a reflection on the relationship between the agencified regulatory model and the concept of democracy. It is important to observe that in complex decision-making processes, the democratic ideal is not usually reduced to the notion of direct participation of the represented ones to choose their representatives, and therefore the elective scheme is not the only democratic manifestation, which seems to be the case of regulatory agencies.

Justen Filho (2011) also points out that democratic legitimacy can take place in different ways, many of which involve the neutralization of most population, as in the criteria for admission of members of the Judiciary, and nominations of the regulatory agencies that are controlled by a system that limits them and against decisions of the tripartite power of the State.

From a structural point of view, the author also points out the following evidences of what he considers to be inferences from the presence of democracy in the agencified regulatory models: (a) the collegiate composition and the joint competences in decision-making processes and in the exercise of the regulatory power of agencies; (b) the possibility of dividing the participation of different political power centers as members of the agencies; (c) the existence of mismatched mandates among the agency directors, which prevents the homogenization of the governing body under the influence of a single political group; (d) objective, technical and scientific criteria for the investiture requirements of executive positions; and (e) fixed term of office, prohibition to reappointment and guarantees against “ad nutum” dismissal of agency directors.

However, democracy is also effective through the improvement of communication channels between the State and the Society, providing participation and integration among the interested parties in the formation of determined and significant decisions.

Thus, from a functional point of view, Asensi (2009) points out that although society's need to participate in decision-making is established, given its technical inability to contribute to the regulatory process, other mechanisms are present to mitigate the excessive technicality and eventual democratic deficit in its decision-making instances, thus setting up what he calls “public spaces for participation”.

Such “spaces” represent an expression of a fragmented, capillary representation of democracy, sensitive to local particularities, acting at micro social level, in a punctual and dialogical way, where spaces of conflict, agreement and negotiation are manifested.

They can manifest in different ways, as for example, (a) due to the possibility of consultations and public hearings, (b) due to the constitution of ombudsmen, or (c) incorporation of social demands in the decision-making process.

In the case of ANVISA, these public spaces take the form of (a) public hearings, (b) public consultations, (c) public subsidy takings, (d) guided consultations, (e) sectorial dialogues and, (f) call notices, institutes that will be detailed in the section on the particularities of regulation in the clinical research segment.

5 PERFORMATIVE APPROACH

Performativity has a transdisciplinary and, therefore heterogeneous trajectory. It is an itinerant concept (CANBATOUS; SERGI, 2018) that covered different areas of knowledge, such as philosophy of language, French post-structuralism, theorizations about humankind, and, especially for the interests of this thesis, the theories produced by STS (Science Technology Studies), of which Bruno Latour and Michel Callon, are the precursors.

Originally, the idea of performativity can be linked to the British philosopher John Austin (1962), in the context of theorizing about language and in his search for the relation between language and truth and between statements and facts.

Austin developed the idea that some statements would not only be suitable to describe a reality, but would be able to to transform or decree the status of a reality. Therefore, one could not only affirm the truth or falsity of a proposition since some of these propositions would have a 'performative' or spreading nature of the declared truths.

The neologism “the utterances”, or enunciations, which are not limited to verifying a fact, but do execute something, was created from these ideas brought by Austin (1962).

According to the example given by Austin (1962), a justice of the peace before a couple that was declared as “husband and wife” not only describes a reality, but decrees it, thus establishing a new marital status. Statements that are pronounced and cause an action or make the listener have a reaction are also performative.

A second perspective on performativity can be found from the works of Judith Butler (1997) that deal with the self-constitution of actors.

This perspective comes from the contributions of Derrida (1979), who opposed Austin by denying that the strength of performativity (or the ability to do things) would come from the authentic intentions of the speaker, who would become an ally to the context in which a speech is handed down. Derrida (1979), on the contrary, stated that the performative force would come from the citation and not from the intention (GOND et al, 2015), since the citation would be the condition of possibility for the intention to operate due to its anteriority.

The performativity advocated by Butler (1999a) would lead to reflection on how humankind could be an expectation that ends up by producing the very phenomenon it anticipated. For Butler (1999a), even the materiality of human bodies could not be elaborated except through discourses, to the point that discourses would shape what we conceive and constitute as a body.

This performative process of constitution of the human race would occur through the reiteration of acts of micro-movements of the body that solidify over time to produce the appearance of substance or a natural type of being.

Thus, no male or female preexists the discursive or material practices they bring about their masculinity or femininity.

More recently, Butler (2010) argued that just as the substantive-metaphysical notion of gender has been overturned by performativity, so economics is the result of processes and practices that produce the effect of what we know as such. With this, organizations, management and strategy should also be seen as converging effects of performative practices (BUTLER, 2010) or their existence could only be recognized from repeatedly constructed micro-movements, or the "enacted" (GUÉRARD et al, 2013).

A third perspective on performativity is found in the work of Karen Barad (2003), which derives from the works of Judith Butler but is also influenced by ANT. Here, performativity goes beyond purely discursive approaches based on the representative power of words to involve the material world of pre-existing things.

Performativity would not be an invitation to turn things into words, but a contestation of the excessive power given to language that gives its place to human and non-human elements in determining the ontologies of reality (BARAD, 2008).

According to Conform Gond and Cabantous (2015), the Baradian version of performativity incorporates the material and the discursive, the social and the scientific, the human and non-human, the natural and the cultural. A post-humanist account is made based on the flow of practices through which borders are stabilized and destabilized.

The fourth and most prominent version of performativity, especially for the purposes of this thesis report, is the one developed by Science & Technology Studies (STS) sociologists represented by Callon (1998), Latour (1996) and Mackenzie (2007), who embraced Austin's idea and also recognized that scientific claims are performative in the sense that they are not outside the worlds they refer to.

The study of the performative role of scientific theories and models was specially explored by Michel Callon in his work "The Laws of the Markets" (1998) when performing a performative analysis of economics, also covering areas related to finance and marketing and management in general.

For Callon (1988, 2007), models and theorizations about markets would not only involve a pre-existing description, but would participate in the configuration of the phenomena they propose to describe, thus constituting them and making them real.

Callon's economic thesis of performativity also suggests that the constitution of the realities described by theorizations involve not only the social sciences, but also the natural sciences, in an indication that converges with Barak's sociomateriality.

Therefore, scientific statements would be associated with the socio-technical arrangements or agencement involved in the production of the facts referred to in these statements (CALLON, 2007). It is as if the technical instruction manual of a device, although being a compilation of the description of the device in question, ends up participating in its constitution because it is the agencement that makes it work (CALLON, 2007).

Agencements are incorporated into the operating statements of a technical device, capabilities are incorporated into the equipment, into the rules and procedures involved, without distinguishing between statements and materiality in this arrangement. Both constitute the elements of an arrangement endowed with agency to give meaning and reality that they propose to describe (CALLON, 2007).

Finally, Callon (2007) argues that the theorizations, more than corresponding to the truths they are intended to predict, are fulfilled with the endorsement of social, political and technical elements, thus constituting the foreseen reality from then on. It is, therefore, a constructivist approach of the participation of heterogeneous elements in the constitution and affirmation of the scientific fact.

In the field of organizational theory, studies that use the performative approach have invariably used all the perspectives listed above to understand different phenomena of the organization.

According to Gond et al (2015), organizational studies based on performativity go in the following directions: a) those based on the Austian perspective that honor the view of discourses as promulgating reality; b) works that emphasize the practices of organizational actors as inducers of emerging strategies; c) researches that emphasize the ontologically procedural nature of organizations, taken by continuous and fluid processes; and d) works on the agencements of material and social elements as constitutive of knowledge and of the organizations themselves.

In defense of a performative mentality for the study of regulation, we propose that this study takes place from the perspective of actor-network theory. This implies affirming that the performative approach, as it is broad and transversal to different theoretical traditions, is not limited only to the version developed by Callon (1998). ANT, in turn, in addition to its initial development based on Latour, Callon and Law, no longer constituted a cohesive body, with almost ten versions or variations of its theoretical body being recognized (KANGER, 2017).

The actor-network theory has its origins in the STS, which is based on materiality and procedurality. As for performativity, whatever approach is adopted, it is relevant to notice that this is not a theory or a method, but a mentality or a “mindset” that permeates various theoretical approaches (GARUD, GEHMAN. THARCHEN , 2018) and which is characterized by two important aspects.

The first aspect is the idea that descriptions "add to reality" insofar as they "instantiate or effect their own referent", and, therefore, "provoke a new situation or ontological agreement" (MUNIESA, 2014, p. 18). The second aspect is in its ontologically relational approach whereby its scholars are not interested in pre-existing, things but in “things happening” and in the “relationships between things” (CABANTOUS, SERGI, 2018).

This aspect is well evidenced in the version of performativity defended by ANT, according to Callon (2007), whose semiotic principle of relationality is not restricted to language or signs, but applies to all types of materials (LAW, 1999).

It is important to observe that there are also intersections between performativity and procedural approaches, and it has even been stated that a performative mentality is inherently procedural (CALLON, 2007). In this regard, Cabantous and Sergi (2018) refer to two commonalities between these perspectives.

The first of them constitutes what these authors call a methodological commitment to qualitative empirical research, aimed at following and describing the action along with everything involved in it, with a view and scrutinizing “what is happening”.

This leads to the second commonality which is the idea that reality is procedural. In any versions of performativity, whether they are interested in discourses, genres or theories or models, and as such phenomena enact the realities with which they are involved, something more than a temporal stability, or some aspect of something that may be will always be implied.

However, for a more precise understanding of these commonalities, it is necessary to understand that there are many approaches to processes, and once again it is necessary to establish relevant distinctions between performativity and procedurality from the intersection of such broad approaches.

The first distinction concerns the agency. While process theories can accommodate various agentic approaches, including those centered on human agency, performative studies will always adopt post-human approaches, precisely with the intention of deconstructing the idea of human intentionality and protagonism to understand reality. It is in this aspect that the approaches to semiotics, derived from STS, Callon's symmetry and Austin's linguistics are invoked.

The variety in the treatment of agency leads to a second difference between procedurality and performativity, which is sociomateriality, well developed by Barad (2003) in his version of performativity. Likewise, the notion of agencement developed by Callon (1998) formed by socio-technical elements evidences this distinctive feature of the performative vision that is not always present in procedural approaches.

The third difference is that while those who study the process emphasize issues regarding change and movement, performativity theorists are concerned with the idea of durability, once the focus is to understand how phenomena become visible or perceptible. In this aspect, the notion of punctuation, derived from ANT (LAW, 2004; LATOUR, 2007) reflects this subtle difference, since the reality constituted by the associations of actors-networks may become recurrences of patterns of movement in networks, reifying in macro-actors or institutional-actors. The inflection point, however, remains a flow activity, which highlights the performative character of ANT, without thereby giving up its procedural and flow ontology.

The fourth distinctive aspect among studies based on process and performativity approaches is the relational issue. While performative approaches come from a relational ontology, such as Baradian and actor-network theories, in procedural approaches, relationality is only compatible with the so-called 'strong theories' of processes, as recognized by authors like Cooper (2005) and Hernes (2014).

Having presented the commonalities, as well as the differences between performative and process approaches, it is also recognized the possibility that studies in performativity are benefited if some aspects of procedurality are incorporated in them (GARUD; GEHMAN; THARCHEN, 2018), now treated as challenges to get the most out of studies in performativity.

The first of them is to avoid the “ballistic pitfall” (MUNIESA, 2018), which consists in looking for causal connections, overly linear trajectories and recursions or circular explanations between the studied phenomena. The performative approach requires a focus on “becoming”, on the multitemporal and multispatial, something that reveals the unleashing of phenomena without the need for clear, defined or finalized trajectories. By avoiding linear conceptualizations, “being” and “becoming” are linked in such a way that the thinking of the process will focus more on transformations and will divert us from a conceptual and stabilized language. The idea is to embrace processuality in performative studies so that we are not stuck in what may appear to be causal or linear explanations.

The second challenge of approaching performativity as a process is to reject the search for causal explanations for performativity itself or the capture of classifications or gradations of performativity, as has been done in some works. When embracing processuality in

performativity studies, attention should be focused on the stabilization processes themselves and not on the results or effects of these processes. It is also important to notice that these stabilizations can be partial and incomplete, but as long as the process forges links between abstractions and material things, then a performative process will be taking place (CABANTOUS; SERGI, 2018).

The third challenge is that there is no need to constitute "proof" of the performativity of the phenomenon being studied. The performative approach does not seek evidence of performativity, since it is enough to shed light on the process or reveal the complexity of its becoming. This implies in "mindset" change regarding the way phenomena are described and a posture ontologically based on fluidity. Materiality itself assumes a spectrum, like a rainbow, and performative narratives may describe phenomena with different natures, which may be a discourse, an idea, a tangible thing or a hydride.

Therefore, the development of a performative mentality implies in investigating multiple and complex relations between statements and ideas among abstractions and their visible tangible expressions (or their materialization), unveiling how phenomena aggregate, disaggregate, stabilize and destabilize in the midst of a fluid process of associations of heterogeneous elements.

Inspired by the work of Villar (2019) and Cabantous (2018), I present a proposal on the particularities of employing a performative mentality for regulation studies from an actor-network perspective.

Through the rhetorical questions specified in the table below, our thesis challenges a substantive ontology to conceive the regulation as the effect of a heterogeneous or socio-technical arrangement that generates performativity on practices subject to regulatory activity.

At the same time, we intend to demonstrate that these practices act to establish a legislative process for the creation of a regulatory legal framework and, therefore act performatively to enact changes in this process approval with no approval of the recommended law up to the moment.

It is as if we could understand regulation from the interrelationships it maintains with other actants (research sponsors, scientists, research participants, ANVISA, the CEP-CONEP system, diseases etc.) and at the same time understand it through intra-relationships that create, modify and recreate the regulatory status (PLS 200, PL 7082, legislative amendments, the new CEP, the new CEI, the "National System of Ethics in Research" etc).

The performative mentality allows us to understand a regulatory dynamic as a network of relations that simultaneously generate performative effects on regulated activities (inter-

relations), and suffer performative effects from the re-creation of its own agencement (intra-relations).

For example, interrelationships are the result of the interactions that regulation has with the heterogeneous networks represented by the pharmaceutical industry, the scientific community and clinical research participants.

Intra-relations, on the other hand, are manifested through the ongoing legislative process aimed at punctuating regulatory inter-relations. All legal and political artifacts of the internal regulations of the Senate and of the Chamber of Deputies, lobbying activities and scientific activities, which involve new discoveries and even new diseases are present.

Performativity is manifested in a bidirectional way since regulatory interrelationships modify intrarelationships as well as the contrary. It is also clear from the heterogeneity, processuality and performativity mentioned above that regulation is now conceived as an effect of socio-technical arrangement (intra-relations) while it mediates the movement of other networks around interests regulated by it (interrelations).

The issues below also help to show how the performative mentality to be developed contemplates the materiality and the processuality in the work of networks involved in regulation:

Table 2 Characteristics of the performative mentality for regulation

<table>
<tr><th></th><th>Performative mentality</th><th>How it manifests</th></tr>
<tr><td>What is regulation?</td><td>Regulation is an effect of a stable agencement (socio-technical arrangement) or network of relations</td><td>It is an effect, but also activates the network of relations that gave rise to it. It changes when the network arrangements that support it also change.</td></tr>
<tr><td>How is the regulatory process constituted?</td><td>It is a movement of heterogeneous networks around a common interest</td><td>It occurs through displacements of actors-networks acting in time and space</td></tr>
<tr><td rowspan="2">What are the movement or trajectory of this process?</td><td>Regulation constitutes and consists of relations mediated by elements of networks that coexist symmetrically</td><td>Regulation has a performative action on the networks it intends to regulate, and also suffers the performative effect of these network elements.</td></tr>
<tr><td colspan="2">Both the regulation (actant) and the process that defines the object of regulation generate effects and suffer performative effects in relation to the other actants or heterogeneous elements that make up the networks.</td></tr>
</table>

Source: Author, adapted from Villar & Cabantous, 2018

Therefore, this thesis proposes to problematize the understanding of the regulatory process based on a performative mentality, based on a post-structural paradigm in which regulation is conceived by a relational and intertemporal ontology of process whose reality is configured by heterogeneous arrangements of multiple actants that associate in the form of actors-networks.

6 THE CLINICAL RESEARCH SEGMENT

It is not an easy task to understand pharmaceutical Research and Development and its economic segments, especially in regard to clinical research and its particularities, and that is the reason for this section.

I also find it necessary to start this section by recovering the concept, development and history of health, as in a post-structuralist and performative view, the past explains the present and involves the future, in a cyclic, circular or spiral manner (LATOUR , 1994).

Thus, the dynamics of clinical research can be understood from the perception of how the concept of health is also procedural, leading us to consider ontologically fluid all realities involved by the research problem: health, health system administration, health economic exploitation, pharmaceutical research and development and, as a consequence, clinical research.

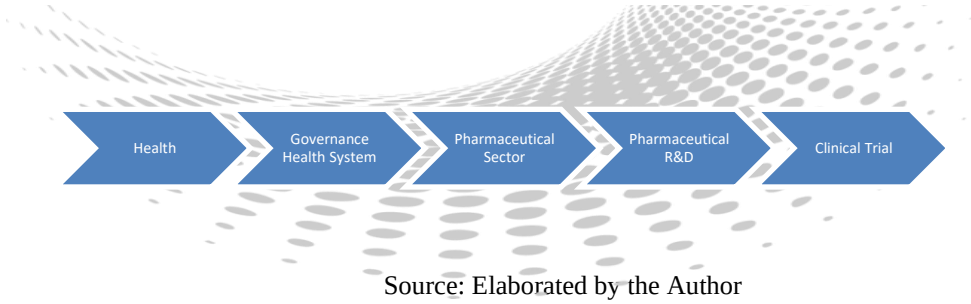
First I provide a more descriptive explanation on how the development of the notion of health gave rise to the recognition of the basic right to it. Second, I demonstrate that the constitutional right to health caused health policies and administrative systems to emerge, thus resulting in the development of an industry of health products and services.

Third, I focus on the pharmaceutical sector, in which the research and development processes (Pharmaceutical R&D) are, and then on the segment that arouse from this process and is the purpose of this paper: clinical research .

Fourth, I analyze the issues concerning competitiveness in the clinical research industry, contrasting them with the regulatory aspects introduced in the previous section.

Finally, I describe the current Brazilian standard regarding regulation of clinical research, through presentation of the Health Surveillance Agency (ANVISA), the National Health Council (CNS), the National Research Ethics Commission (CONEP), the Councils of Ethics in Research (CEP), besides the international guidelines on regulation followed by this standard.

Figure 11 Ontological view of Research Clinical



Source: Elaborated by the Author

6.1 Procedural analysis on the concept of health

I begin this section with a personal statement: although death is unavoidable, it causes resignation and rejection, to the point that among existential needs, the notion of protecting life and the struggle for longevity perhaps constitute the most basic interests.

Several existential, behavioral, political, social and even economic processes are a result of this, involve this subject and somehow create an interest in making life longer (or postponing death). Here I highlight some of the processes affected by the issues involved in this thesis.

The concept of health (and illness) reflects an economic, political and social situation. There is no single or static concept, but temporal and spatial variations on what it can mean (SCLIAR, 2007).

In ancient cultures, disease was associated with the action of forces external to the organism as a sign of disobedience to divine command. Take, for example, the case of leprosy, considered a curse among the Jews, as recorded in the Christian bible in the book of Leviticus chapter 14, verses 54 to 57.

In ancient times, Greek medicine began to face disease in a different way thanks to one of its exponents, Hippocrates of Kos (460-377 BC), known as the "father of medicine". His writings reflect a more rational view, in which diseases occurred due to natural causes. For him, health would be based on the balance of four main fluids in the body (yellow bile, black bile, phlegm and blood). The disease, in turn, would be considered a disorganization of this humoral state. Hippocrates valued empirical observation, which was understood as an embryonic approach to what would later constitute the epidemiological view of the health-disease problem (SCLIAR, 2007).

Later, Galen (129-199 BC) revisited Hippocrates's humoral theory and, although emphasizing the importance of the four temperaments in health, considered to have endogenous

causes, he also included exogenous causes associated with physical constitution and habits of human life.

In the European Middle Ages, the influence of the Christian religion maintained the conception of illness, as a result of sin and healing, and as a matter of faith. At that time, the care of the sick was trusted to religious orders or their hospitals and focus was more on shelter and comfort than on the treatment or cure of patients.

Christianity also emphasized the ideas of Hippocrates and Galen, with a prophylactic approach: disease could be avoided through temperance in eating habits, sexual restriction and control of passions (SCLIAR, 2007).

Modernity has significantly changed the concept of health. With the development of alchemy, Paracelsus (1493-1541) argued that since the processes taking place in the human body are chemical, the best remedies for expelling disease must also be chemical. It was then that patients received small doses of metals and minerals, such as mercury, used to treat syphilis, which has become epidemic in Europe (SCLIAR, 2007).

Under the development of mechanics, Descartes, who postulated mind-body dualism, understood analogically that the body would function as a "machine". Later, with the development of anatomy, François Bichat (1771-1802) removed the humoral conception of the disease, which would be located in human organs.

Interestingly, despite the progress in fighting disease, Pascal said that disease would be a way of understanding what life is, of accepting death, and especially God. Chopin, for example, claimed that illness would refine the art of living and that under certain circumstances health would even be dispensable (SCLIAR, 2007).

In the 19th century the “Pasteurian revolution” occurred, and through the microscope the existence of microorganisms that caused disease was discovered, thus generating the development of serums and vaccines. It is important to highlight that there was no progress, except for the non-human agency in the process. From that moment on the etiological factors of the disease could be identified and the disease could be prevented and treated.

Such knowledge stimulated tropical medicine, whose objective was to control endemic and epidemic transmissible diseases, mainly motivated by threats to commercial companies that emerged in the context of the colonial expansion of the 17th century Europe.

The contribution of John Snow (1813-1858) was decisive for the emergence of epidemiology, also known as “disease accounting”. The aim was to control health through indicators (not of a single organism only, but in a social scope).

According to Scliar (2007), epidemiology was one of the great drivers of statistics, which was then a new science not so common in the modern world. Data on population, education, production and income level were collected. The relation between these data and the levels of urbanization and proletarianization, along with the understanding of their effects on health, became statistical surveys that resulted in a period of reports concerning violation of basic rights.

From the statistical control of health, it was possible to identify inequalities between "healthy" and "unhealthy" districts in England during the industrial revolution period.

In 1848, the English Parliament enacted the "Public Health Act", which created a General Board of Health, mainly to propose public health measures and recruit doctors. The first steps were taken to design the concept of a System of Public Health Administration in Great Britain.

However, a large pioneer program of social security and health was created in Germany, in 1883, by Oto von Bismarck. The system was later implemented in France and copied by several other countries around the world.

A paradigm shift would take place in Britain during World War II. To compensate post-war suffering, the British government used public money to offer "National Health Service" to the whole population.

A consensus regarding universalization of health care spread worldwide after the creation of the United Nations (UN) and the World Health Organization (WHO), whose charter of principles, dated of of April 7, 1948, established the right to health and the obligation of the State in its promotion and protection.

The scope of health concept adopted by the WHO received severe criticism (SCLIAR, 2007). From a technical point of view, establishing the right to health in universal terms would be something utopian or unattainable. From a political and libertarian point of view, universalization would put the individual rights of citizens at risk under the pretext of promoting health.

The path to universal health, however, did not happen suddenly, but developed gradually. In its first actions, WHO developed programs for the eradication of communicable diseases with a high potential for morbidity and mortality: malaria and smallpox (WHO, 2010). Subsequently, its objectives were considerably expanded, influenced mainly by the demand of socialist countries, which played important roles in that period.

Emphasis was on the responsibility of the government to provide health and the participation of people and communities in planning and implementing health care. The base of the new vision brought by WHO were: (a) actions concerning health must be practical,

achievable, accessible and socially acceptable and (b) services cost must be proportional to the economic situation of the region and country. Therefore, it was established that primary health care services represent the principle to the health system, constituting its base.

On the other hand, a national health system must be fully integrated to the process of social and economic development of the country, which process is a cause and a consequence of health. The issue was to understand what the concept of "primary health care" was, which is something that concerns each country that adopted its own health system.

In Brazil, for example, the Constitution of the Republic of 1988 avoids discussing the concept of health (MAPELLI JR, 2008), but states in its article 196 that:

> "Health is everyone's right and a State obligation, guaranteed by social and economic policies concerning decrease of the risk of disease and other damages, and universal and equal access to actions and services for promotion, protection and recovery".

Key issues remain regarding the extent and limits of the right to health, economic implications of technologies developed for health care, and how it is financed. As a reflection of the new vision of universal health care, Brazil, in its Federal Constitution of 1988, changed profoundly the way it started to provide health services to its population (MAPELLI JR, 2008).

During the period in which it lived under the military regime (from 1964 to 1987), Brazil kept a sanitary model aiming basically the control of safety against diseases that harmed foreign trade, which was predominantly represented by the export of agricultural "commodities".

Then the country adopted a private-assistance model that guaranteed the immunization of the population that lived in large centers and offered services in private hospitals to assist formal workers and contributors of the health system.

Although this second model was more inclusive than the previous one, its contributory aspect still prevented a large part of the Brazilian population to benefit from public health services. This caused a lot of questioning, and pressure began for the right of health-related services and care universalization. This began in the 1980s and is known as the sanitary movement.

This movement was incorporated to the Brazilian democratization process and health was finally recognized and established at constitutional level as a social right and an obligation of the State, as defined to this day.

Then, in 1988, the Unified Health System was created. It consisted of a set of policies aimed at reducing the risk of diseases and universal and equal access to actions and services for its promotion, protection and recovery (LENZA, 2008).

From 1988 on, health became a basic right, which meant that the whole Brazilian population would have financial protection from the State, guaranteed by a Federal Constitution providing payments concerning sickness costs (MENDES, 2017).

This new legal health conception, along with the creation of a universal health care system, caused a series of controversies whose performance is worth mentioning.

According to Wang et al (2016), the Brazilian population in general was able to gradually experience the positive impact that universalization had on human and social development indicators. Little by little they understood the benefits of gratuity and increased pressure for the establishment of these rights.

It was also recognized that the improvement in life quality raised the levels of longevity of the population. However, this circumstance caused the system to become overloaded, considering that the population's needs were increased, which would undergo an aging process with increase on demands and costs.

Increase in demand has caused the pharmaceutical sector to increase research and development of new drugs, in a growing search for new technologies and the aim of treating more rare and specific diseases.

Challenges were not only focused on controlling infectious diseases, as in the sanitary model of the 1950s, in which life expectancy was of 48 years in average.

Life expectancy is now superior to 72 over years, and this number is going to increase by one year each year, thus focus would be on people's well-being and improvement of the existing therapies upon reduction of side-effect reactions and access to treatment.

Pharmaceutical research and development (R&D) would also deal with new demands and promote significant advance to control diseases such as AIDS, Hepatitis C and some types of cancer. Finally, these demands would include future challenges connected to the recent findings of biotechnology, thus enabling genetic sequencing and decoding, and providing personal and sophisticated treatments.

However, dilemmas arose about how limited government health resources could support the rising costs of medical technology applied to the research and development of new drugs.

Some important movements resulted from this process: (a) on the one hand, the pharmaceutical R&D industry adopted new strategies to reorganize its activities and face the quantitative and qualitative increase in its demand; (b) on the other hand, government requirements were also increased through an intensive regulatory policy on the practices of the pharmaceutical sector.

6.2 The pharmaceutical R&D industry and the clinical research segment

The pharmaceutical sector, which involves R&D processes, is one of the most complex and costly industries in economic activity. It can take more than 10 years for a new product to be launched and US$ 1 billion of investment can be spent to do so (BERNDT et al, 2005).

Data from the Pharmaceutical Research Industry Association - INTERFARMA (2020) show that global investment in pharmaceutical R&D has grown 4.4% annually from 2013 to 2018, with a total investment of around US$ 172 billion in 2018 and a forecast of reaching US$ 200 billion in 2023.

INTERFARMA (2020) estimates that from 100,000 new compounds discovered, only 250 are submitted to pre-clinical tests, five of these are submitted to clinical trials, and only one reaches the market. It is necessary to explain how the pharmaceutical R&D process takes place in order to understand what clinical research consists of.

According to Gomes et al (2012), R&D for new drugs involves a series of three steps that start from “basic research”, going through the phase of “pre-clinical trials” (also known as “non-clinical trials”) reaching the “clinical trials” or “clinical research” or “clinical tests”.

In short, the first step regards “basic research”, which involves the activities necessary to identify promising compounds and molecules for the treatment of a disease. At this stage, many compounds are investigated and a relevant part of the research is carried out in universities, institutions and research foundations.

The second step, called "non-clinical studies" or "pre-clinical tests", constitutes the continuation of the basic research, in which the active compounds are tested in vitro or in animals to evaluate the parameters of safety and efficiency the new compound.

The third step is “clinical testing” (or “clinical trials” or “clinical research”) and aims to obtain evidence regarding how safe and efficient it is to use the product in human beings. This step is divided into four phases.

Phase I aims to verify the tolerance and safety of the new drug by administering dosages to a small number of healthy volunteers.

Phase II checks the short-term effectiveness of the drug to treat the target disease in patients who present the disease to be treated, generating information about safety, adverse effects and potential risks.

Phase III aims to assess the risk-benefit of the treatment, usually in a comparative way versus placebo or using another reference treatment. It usually has hundreds or thousands of participants who have the disease.

Phase IV is also called post-marketing research, and starts after the regulatory agency approves the product to be marketed. At this stage, the effects and unexpected adverse reactions of the drug must be monitored. This monitoring process, called “medicine surveillance”, is carried out by the company responsible for the product in accordance with the respective health standards.

Among all the steps mentioned above, step III comprises the most expensive and time-consuming stage of the drug development process. This is mainly due to the growth in the number of biotechnological medicines under development, with processes that are increasingly expensive and complex.

Therefore, we can define a clinical research as a step in the R&D process that consists of investigating the effects of treating a group of human beings with a new product. The targets are to prove its safety and efficiency, evaluate the recommended dose of the product and check possible occurrences of adverse effects (GOMES et al, 2012).

The ability to develop new drugs can be directly related to the skills to carry out these tests, and this led to a high vertical integration of the research and development process in the pharmaceutical industry throughout the 20th century.

Data from INTERFARMA (2020) shows that clinical research has a large stake in the total investment in (R&D). It estimated that pharmaceutical R&D investments in the US for the whole year of 2018 were: US$ 36, 50 billion in basic and non-clinical research, $111.6 billion in clinical research and $23.9 billion in uncategorized investments.

Historically, the business model of the R&D sector has remained predominantly vertically integrated, although the existence of alliances between the pharmaceutical industry and universities was recurrent (especially for the stages of basic research), and hospitals that provided the locations for clinical trials (GOMES et al, 2012).

This configuration began to change in the 1980s, with the emergence of modern biotechnology outside the large R&D centers of large pharmaceutical companies. This change had to do with the fact that universities did not generally have the necessary structure to develop innovative molecules.

In this context, pharmaceutical companies have established two deliberate strategies. The first one was having partnerships with biotechnology companies. The second, resulting from the first, was the reorganization of pharmaceutical R&D management, with companies now acting as contract managers with other companies specialized in specific stages of the process, such as biotechnology companies, CMOs (Contract Manufacturing Organizations) and CROs (Contract Research Organizations).

More recently, the levels of vertical disintegration of pharmaceutical R&D have increased due to technical, financial and regulatory pressures that the industry had been facing in recent years (INTERFARMA, 2020).

From a technical point of view, demands for treatments of more complex, multi-symptomatic and multi-factor diseases, whose clinical evaluations are longer and more costly has grown. The number of molecules tested in the initial stages of the process also increased, which was reflected in an increase in the number of clinical trials, a need to manage product portfolios and the generation of competing projects for the same type of treatment.

Greater competitiveness, associated with the factors listed above, led the sector to live with financial pressures due to having less credit for research. Financing agents such as companies and venture capital funds became more discerning and demanding, seeking greater security in analyzing their investments return.

Finally, regulatory pressures became a crucial factor for pharmaceutical R&D, which began to live with increasing requirements, resulting in the extension of deadlines for approval of the stages of the process, increased supervision and expansion of the regulatory scope with implications and ethical questions about conducting research.

The intensification of regulation of clinical research activities has an explanation. According to the "Center for Information and Study on Clinical Research Participation (CISCRP)", the increase in regulatory pressure was an effect of the failures of the R&D process evidenced in recent years, being recorded by GBI Research (2011) that in the market of North America and Europe more than 130 drugs were withdrawn from circulation due to adverse effects that were not identified in the clinical stage of their development (GOMES et al, 2012).

Concretely, the main strategies used by pharmaceutical companies to face technical, financial and regulatory pressures have been off shoring and outsourcing, which can occur alone or simultaneously and involve any stage of the process, although it is recognized that these strategies were more intensive in stage of “clinical research”, as they are longer, more expensive and labor intensive (GOMES et al, 2012).

Through off shoring, or internationalization, a company transfers the infrastructure responsible for carrying out a certain activity abroad, where it will be performed in the same way, taking advantage of cost, regulatory, tax and labor advantages, among others (HUIJSTEE et al, 2011).

The internationalization of pharmaceutical R&D represented a significant opportunity for the insertion of developing countries into a production chain with high technological density and added value.

According to the 2015 “Biopharmaceutical Industry-Sponsored Clinical Trials - Impact on State Economies” report, prepared for the Pharmaceutical Research and Manufacturers of America (PhRMA), the main internationalization destinations have been South Korea, China, India, East European and Latin America (HUIJSTEE et al, 2011 apud GOMES, 2012), whose main competitive advantages are linked to the ease in capturing patients and the lower cost of the test per patient, factors that are also linked to the fragility of health systems in these countries whose population sees participation in a clinical trial as a way to obtain better health care.

Outsourcing involves the hiring of a specialized company by another, called borrower, to carry out the activities of its operation on behalf of the borrower.

Most of the pharmaceutical industry's R&D outsourced activities are carried out by CROs (Contract Research Organization), which can provide pre-clinical testing, laboratory analysis, formulation, regulatory advice, clinical trials and post-marketing studies.

The advantages of the outsourcing process are well known, with emphasis on the estimated 30% reduction in total testing time and access to knowledge from various sources external to the organization, which contributes to the success rate and faster identification of probable failures (FROST & SULLIVAN, 2010 apud GOMES, 2012).

Thus, united both strategies, multinational companies, especially North American ones, created a very competitive international market to attract and carry out clinical trials, particularly in developing countries, such as Brazil, giving rise to a market for services technologies with their own characteristics, dynamics and actors, whose estimated size is around US$ 112 billion per year, or the equivalent of around 65% of all private global investment in R&D in the pharmaceutical sector, in the amount of US$ 172 million performed in 2014 (INTERFARMA, 2020).

Relations among CROs and the pharmaceutical sector also proved to be extremely dynamic, sometimes towards outsourcing and sometimes reversing this movement, causing some CROs to get closer to pharmaceutical companies by means of partnerships, strategic alliances, joint ventures and even mergers.

Despite the significant numbers that place Brazil in the ranking of the 6th largest pharmaceutical market in the world, in terms of clinical research it ranks the 24th, with only 2.1% of studies carried out in 2018.

An even more relevant fact is that in the last 10 years the country has lost seven positions in this ranking, which shows a constant movement of competitiveness loss (INTERFARMA, 2020).

There is an emphatic defense regarding the relevance of the clinical research market, and there are several benefits to countries that offer proper conditions for its realization: attracting investments and increasing the country's economic activity, leveraging scientific production and innovation; increased access to health (INTERFARMA, 2019).

Other factors are considered when defining the countries where a study will be conducted with emphasis on logistical complexity of carrying out the study, level of preparation and professionalism of the research centers, estimated time for approval and execution of the study, epidemiology in the country of the disease being researched, prevailing therapeutic approach in the country, robustness of the regulatory and ethical environment and execution cost.

6.3 Clinical research in Brazil and the challenges of competitiveness

According to INTERFARMA (2020), Brazil has a set of characteristics that could make it an absolute reference to conduct clinical studies.

First, the country is populous (around 220 million inhabitants) and economically relevant (9^{th} largest GDP), there is a high population concentration in urban areas (182 million) and it has a relevant pharmaceutical market (7^{th} position in drug sales volume).

Its diverse ethnic composition also stands out, as its ethnic fractionalization index is higher than that of countries like the United States, Argentina, Australia, the largest countries in Europe and Asia (ALESINA et al, 2002, apud INTERFARMA, 2020), which enables to obtain a variety of genotypes, something considered a critical factor for some specific types of studies relevant to the research.

The costs for carrying out clinical studies in Brazil are comparatively lower than those carried out in other competing countries in Latin America, the United States and Europe considered as reference (INTERFARMA, 2020).

The clinical research system in Brazil has a high level of professionalization and seriousness, involving capable people and institutions, with an internationally recognized reputation, including: sponsors, regulatory agencies, ethics committees, researchers and a multidisciplinary network of technicians and scientists (GOUY et al, 2018).

However, according to the report "The importance of clinical research for Brazil", produced by INTERFARMA (2020), studies sponsored by the pharmaceutical sector have shown that Brazil is still in an unfavorable competitive position in relation to the main players in the segment.

Among the causes of the low competitiveness of the Brazilian clinical research segment, the following stood out:

a) Approval takes longer than in countries like the USA, Poland and Argentina. This happens when we compare deadlines previewed in law, since legally Brazil has one of the longest periods for regulation. It also happens when we consider the periods for approval of the researches performed in the last three years, a ranking in which brazil is in the worst position among those analyzed.

b) The ethical body linked to the National Health Council (CNS), which works together with the Research Ethics Committees (CEP) and the National Research Ethics Commission (CONEP) usually adopts discretionary criteria that result in uncertainty regarding issues already clarified by the regulation parameters.

c) There is a deficit of resources in the health regulator. Structural problems were pointed out in relation to the lack of civil servants to fully meet the demand received by regulatory agencies. Such situation would reinforce the explanation as to why the actual approval time is much longer than the deadlines foreseen by regulatory standards.

d) Brazilian regulatory authorities often formulate atypical and unintelligible requirements during the process of research approval, which is a factor that prevents the country from taking part in clinical research.

6.4 Clinical research in Brazil and the safety bias

The defense of the regulatory status has been forceful and has been formulated by agents who administer or are involved in the process of constitution of regulatory bodies and with the improvement of these bodies over decades.

Failure involving slowness of clinical research is recognized by the agencies, but, according to the conclusions of the Brazilian Society of Clinical Research Professionals (SBPPC) the cause for it is not related to the regulatory issue:

a) Brazil lacks qualified labor to work in the clinical research sector, research centers are not always equipped with the necessary infrastructure to carry out the work and Brazil has logistical problems related to import and export processes that make the release of necessary resources very slow.

b) Not only regulatory deadlines are slow, but pressure to discover new products, involving pharmaceuticals, food and cosmetics has been increasing frantically. People benefit from technological advances, but longevity and improved quality of life make

these achievements relentless. There is an increase in the urge of more effective medications that cause fewer adverse reactions, less drug interactions, and demand from research centers. Researchers search to improve the process of scientific validation to have their findings recognized as soon as possible.

c) Basic concepts regarding process efficiency cannot override the safety and ethics of the research. Delay in analyzing a project is directly proportional to the strictness used to analyze it and the concern relating those who will be part of the research.

The 5th National Meeting of Research Ethics Committees (ENCEP) defends an idea that has been widely used to advocate the regulatory status of Brazilian clinical research. The 5th ENCEP argues that an eventual flexibilization of regulation would expose research participants to the interests of sponsors, who would then be guided by economic interest, wild capitalism and profit.

6.5 Brazilian regime of regulation of clinical research

This project aims to investigate the performativity of the regulatory process of clinical research from the perspective of ANT. It is, therefore, necessary to understand the regulatory regime of this economic segment, which implies the action of the two main entities, now acting in the process, the first one with an ethical scope and the other with a sanitary scope.

There is an important difference between ethical and health regulation. Ethical regulation is present every time a research involves human beings, and it aims at protecting rights, safety and the well-being of those participating in the study, while health regulation regards the control of the research and its registration so that it is introduced in the market.

In this section we will present the structures and regulatory standards of the National Health Surveillance Agency (ANVISA), of sanitary scope, in addition to the National Research Ethics Commission – (CONEP) and the Research Ethics Committees – (CEP), both members of the CEP-CONEP system that belong to the structure of the National Health Council (CNS).

6.5.1 National Health Surveillance Agency - ANVISA

The National Health Surveillance Agency (ANVISA) was created by Law 9.782 of January 26, 1999 and is regulated by Decree 30.169 of April 16, 1999. According to, articles 4 and 5 of Law 9782/99, ANVISA is a special autarchy, characterized by administrative independence, stability of its directors and financial autonomy.

ANVISA is responsible for formulating and executing health regulation to conduct clinical trials in the country. Its main attributions are to implement and monitor clinical trials, notify adverse events, grant import licenses, approve the study and sites of execution and evaluate methodological criteria of the clinical protocol.

As per article 6 of Law 9782/99, the institutional purposes of ANVISA are to protect the population's health, through the sanitary control of the production and consumption of products and services subject to sanitary surveillance, including environments, processes, inputs and technologies related to them, as well as control ports, airports, borders and customs enclosures.

Article 7 brings 28 items regarding attributions of ANVISA. From those we can highlight, due to the scope of these attributions, its competence to establish standards, propose, monitor and execute health surveillance policies, guidelines and actions (item III), besides being able to establish norms and standards regarding the limits of contaminants, toxic residues, disinfectants, heavy metals and others that involve a risk to health (item IV).

The responsibilities arising from ANVISA's surveillance power, defined as an activity of the State that consists of limiting individual rights in benefit of the public interest, linked to clinical research activities, involve the following attributions: granting product registrations according to the rules of its area of expertise (item IX), grant and cancel the certificate of compliance with good manufacturing practices (item X); coordinate health surveillance actions carried out by all laboratories that make up the official network of quality control laboratories in health (item XVII); establish, coordinate and monitor toxicological and pharmacological surveillance systems (item XVIII), and promote the periodic review and update of the pharmacopoeia (item XIX).

According to article 8 of Law 9782/99, among the goods and products subject to sanitary control and inspection by the Agency, there are medicines for human use, their active substances and other inputs, processes and technologies (item I); sets, reagents and supplies for diagnosis (item V); medical-hospital, dental and hemotherapeutic, laboratory and imaging diagnostic equipment and supplies (item VI); immunobiologicals and their active substances, blood and blood products (item VII); human and veterinary organs, tissues for use in transplants or reconstitutions (item XVIII); radioisotopes for in vitro diagnostic use and radiopharmaceuticals and radioactive products used in diagnosis and therapy (item IX); and any products that involve the possibility of a health risk, obtained by genetic engineering, by another procedure or even subjected to radiation sources (item XI).

Paragraph 3 of article 8 also states that the sanitary surveillance regime covered by ANVISA involves all physical facilities, equipment, technologies, environments and

procedures involved in all phases of the production processes of goods and products subject to control and inspection sanitary, including destination of the respective waste.

ANVISA's organizational structure is regulated by articles 9 and the following ones, which provide for a Collegiate Board and an Advisory Board. In Article 5 of its Regulation (Decree 3029/1999) it is stated that the basic structure of the agency has a Collegiate Board, an Attorney General Office, Internal Affairs Office, Ombudsman and an Advisory Board.

For project research purposes the Collegiate Board and the Advisory Board will be emphasized. Both are constituted and disciplined by Law 9782/99 and its regulation.

The Collegiate Board has five members who are appointed by the President of the Republic after prior approval by the Federal Senate; their term is of five years and reelection is prohibited.

Members of the Collegiate Board of Directors are also prohibited to engage in any other professional activity, business, union or political party direction. They are not allowed to have directly or indirectly interest in any company related to Sanitary Surveillance. Restrictions known as “quarantine” are also imposed, which means that after leaving the office the directors are forbidden to represent any person or interest before the Agency for a period of one year.

The Collegiate Board has broad powers, listed in article 15, among which the following stand out: define the Agency's strategic guidelines (item I); propose to the Minister of State for Health the government policies and guidelines aimed at enabling the Agency to fulfill its objectives (item II); edit rules on matters within the Agency's competence, which must be accompanied by technical justifications and, whenever possible, studies of economic and technical impact on the regulated sector and impact on public health, this requirement being waived in cases of serious risk to public health (item III); comply with and enforce the norms related to health surveillance (item IV); prepare and disseminate periodic reports on its activities (item V); judge, at appeal level, the Agency's decisions, upon provocation by the interested parties (item VI);

The Advisory Board is of relevant importance for the purposes of this research project, as it represents society's institutionalized participation body in the basic structure of ANVISA. It has twelve members appointed by representative bodies of the federal, state and municipal government, in addition to entities such as the National Confederation of Industry, National Confederation of Commerce, Scientific Community, National Health Confederation and Associations that represent Consumer Protection (article 17, Regulation).

Pursuant article 18 of the Regulation, the Advisors may remain as members of the Advisory Board for a period of up to three years, and reelection is prohibited. Among other

attributions, they are responsible for the proposal of guidelines and technical recommendations on matters within the Agency's competence (item I), give an opinion on government policy proposals in the Agency's area of operation (item II), consider and issue an opinion on the annual reports of the Collegiate Board (item III); request information and make proposals within the scope of ANVISA's general competences (item IV).

ANVISA's public participation mechanisms constitute the spaces for the external manifestation of interested parties in the decision-making process of ANVISA's institutional competences.

Among the mechanisms stand out (a) public hearing, provided by Law and Decree 3029/99, besides other instruments created by ANVISA within the scope of its normative competence, which are: (b) Public Consultations, (c) Public Grants, (d) Directed Consultations, (e) Sectorial Dialogues and (f) Call Notices.

Pursuant article 33 of Decree 3029/99, public hearing is an important mechanism for popular participation in the Agency's activities and must be carried out with the objective of collecting subsidies and information for the decision-making process of the Agency (item I); provide agents and consumers with the possibility of forwarding their claims, opinions and suggestions (item II); identify, as broadly as possible, all aspects relevant to the subject matter of public hearing (item III) and publicize the Agency's actions (item IV).

According to article 32 of Decree 3029/99, at the discretion of the Collegiate Board public hearing may also be designated to precede the decision-making processes for registering new products, goods and services, as well as the procedures for editing standards according to their characteristics and relevance.

Public Consultation is a mechanism for social participation open to the public and aimed at receiving written contributions regarding a draft of a normative act, document or relevant subject. The manifestations received do not have a decision-making nature and, therefore, are not counted as votes, but as subsidies and information from society for the decision-making process by the board of directors of the Agency regarding the text of the normative act.

Public Consultation is carried out at the advanced stage of the regulation process, when there was already the option for a normative instrument and the draft of a regulatory instrument was drawn up. It is carried out whenever there is a need to fully validate a regulatory text, and is an important mechanism to highlight any necessary adjustments in the normative text before deliberation and publication of the final version of the regulatory draft.

Public Subsidy Taking (TPS) is a consultation mechanism, open to the public, to collect data, information or evidence, in writing, on the Preliminary Regulatory Impact Analysis (RIA)

Report. TPS asks questions about information contained in the AIR Report: regulatory problem to be solved, regulatory options to achieve the intended objectives and identification and comparison of its impacts, as well as implementation and monitoring actions.

The Directed Consultation is a mechanism that seeks information, evidence and data, through questioning the agents involved and affected by regulatory action. Directed Consultations are mainly aimed at a specific audience, such as health surveillance, segments of the regulated sector, areas of Anvisa, academic members and researchers, among others. However, it can also be a mechanism open to any interested party wishing to express their opinion on the subject discussed.

Directed Consultation can be carried out at any time during the regulatory process in order to expand available evidence and collect data or even validate information initially raised.

Sectorial Dialogue is a face-to-face or virtual meeting, held with the aim of quickly validating information collected in the regulatory process, also gathering demands and scenarios that have not emerged yet. These are more informal meetings, with a flexible nature, and may or may not be directed at a more restricted audience. In this sense, several sectorial dialogues can be held with the different segments of agents affected in the regulatory process under discussion.

While Directed Consultations require publication in official newspapers, Sectorial Dialogues, given their informality and flexibility, do not require such action.

Finally, the Notices are not participatory mechanisms, but instruments for calling society to participate in some of the mechanisms for social participation in regulation. The publication of Call Notices must be carried out for the Public Granting of Subsidies and the ICH Regional Consultation; it is optional to other participation mechanisms.

ANVISA, among its competences, has a broad regulatory power that until 2019 resulted in the creation of about 1000 standards of the most varied types, such as Resolutions (RD), Resolutions of the Collegiate Board of Directors (RDC) , Resolutions of the Medicines Market Regulation Chamber (CMED), Ordinances (PRT), Joint Normative Ordinances (PRTC), Normative Instructions (IN) and Joint Normative Instructions (INC).

This excessive proliferation of rules triggered a reaction, so that in the name of the efficiency that gave rise to the agencified model, the same principle is now invoked to seek regulatory optimization, with a view to correcting regulatory excesses.

For this reason, ANVISA started to periodically review its normative acts in order to eliminate obsolete acts; this procedure is called the “Regulatory Guillotine”, which is a mechanism to identify and revoke normative acts that are no longer effective for society.

Anvisa has already carried out three regulatory guillotines since 2016, resulting in the revocation of 349 standards, which correspond to approximately 1/3 of the Agency's Regulatory Inventory in the period. The following diagram presents the results of each.

Figure 12 Regulatory Guillotine

Fonte: Anvisa (2020)

6.5.2 The National Health Council (CNS) and the CEP-CONEP system

The ethical evaluation of a clinical trial involves protecting the rights, safety and well-being of participants in a clinical trial.

This function is carried out by the National Health Council (CNS), which is a deliberative permanent collegiate body of the Unified Health System (SUS) that has 48 (forty-eight) board members and their respective first and second alternates, represented by members of the Ministry of Health, besides user segments, workers, SUS managers, health service providers, social movements, governmental and non-governmental institutions, health professional entities, the scientific community, service provider entities and business entities of the health area.

Created in 1937, CNS's attributions are currently regulated by Law 8142/90. Besides regulating issues related to ethical aspects of clinical research, it is also responsible for formulating strategies and controlling the execution of health policies in Brazil. Its mission is to inspect and monitor public health policies in their different areas, taking the demands of the population to the public authorities, reason why it is called health social control.

In 1996, through Resolution CNS 196/96, CNS established a structure and a process for the ethical evaluation of clinical research, divided in two more stages or approval sub-bodies, whose functions were assigned to two bodies: the National Research Ethics Commission

(CONEP) and the Research Ethics Committees (CEPs) that together constitute what is commonly known as the CEP-CONEP System.

CONEP is a commission created with the aim of implementing the standards and regulatory guidelines for research involving human beings.

CONEP works together with a network of more than 800 Research Ethics Committees (CEP), organized within the institutions where research is carried out.

Therefore, any research protocol involving human beings will be submitted to a CEP, which will have primary responsibility for deciding on the ethics of the research to be carried out at the institution.

Subsequently, if the research project fits into one of the special themes (such as human genetics, human reproduction, new health devices, research on indigenous populations, research conducted abroad and biosafety research), the research protocol will also be submitted to the control of CONEP.

Besides the dual instance of ethical control, for special themes CONEP also acts as an instance to judge appeals against decisions, issued by CEP that disapproved research protocols deemed contrary to the ethical parameters stipulated by the system.

The table below consolidates the evolution of the resolutions issued by the CNS, which refer to the performativity of the CEP-CONEP system, relating to the segment of clinical research in Brazil.

- CNS nº 001/98 - Health Research Standards
- CNS nº 196/96 - Guidelines and Regulatory Norms for Research Involving Human Beings
- CNS No. 222/97- Resolution on the Research Ethics Committee
- CNS nº 240/97- Defines user representation in CEPs and guides the choice
- CNS nº 251 - Comprises the complementary norm for the special thematic area of new drugs, vaccines and diagnostic tests and delegates to CEPs the final analysis of projects in this area, which is no longer special
- CNS nº 292/99 - Establishes specific norms for the approval of research protocols with foreign cooperation, maintaining the requirement of final approval by CONEP, after approval by CEP
- CNS nº 301/2000 - Regards the position of CNS and CONEP against amendments to the Declaration of Helsinki

- CNS nº 303/2000 - Comprises a complementary norm for the area of Human Reproduction, establishing sub-areas that must be analyzed at Conep and delegates to CEPs the analysis of other projects in the area
- CNS nº 340/2004 - Approves the Guidelines for Ethical Analysis and Processing of Research Projects in the Special Thematic Area of Human Genetics
- CNS nº 346/2005 - Multicentric Projects
- CNS No. 347/2005 - Approves guidelines for ethical review of research projects involving storage of materials or use of materials stored in previous research
- CNS nº 37/2007 - Registration and accreditation or renewal of registration and accreditation of CEP
- CNS nº 404/2008 - Declaration of Helsinki
- CNS nº 421/2009 - To institute restructuring in the composition of the National Research Ethics Commission – CONEP
- CNS nº 446/2011 - Composition of the National Research Ethics Commission
- CNS nº 441/2011 - Approve the following guidelines for the ethical review of research projects involving storage of human biological material or use of material stored in previous research
- CNS nº 466/2012 - Approves the guidelines and regulatory standards for research involving human beings and revokes CNS Resolution 196/96
- CNS nº 506/2016 - Regarding the accreditation process of Research Ethics Committees (CEP) that make up the CEP/CONEP System
- CNS No. 510/2016 - Provides for the standards applicable to research in Human and Social Sciences
- CNS nº 563/2017 - Right of research participant with ultra-rare diseases.
- CNS nº 580/2018 - Strategic Research for SUS.
- CNS No. 647/2020 - Provides for the rules regarding the regulation of the designation process and performance of CEP members appointed by social control entities
- CNS nº 656/2021 - Provides for the extension of the mandate within the National Research Ethics Commission of the National Health Council.

Although ethical and health regulations have different scopes, the simultaneous action between the regulations can lead both instances to a situation of overlapping competences. For this reason, any ethical issues identified by ANVISA are frequently referred to CONEP.

6.5.3 International Guidelines on the Regulation of Clinical Research

There are two international guidelines for research on human subjects, which are periodically revised.

The first of them is the Declaration of Helsinki, whose main contribution was the introduction of the Ethics and Research Committees (CEP), and served as a parameter for the institution of the CEP-CONEP system in Brazil, and was instituted to ensure that (a) the benefits of the study outweigh its risks, (b) participants are informed of their rights and risks involved, and (c) there is no pressure to participate.

The second represents a set of principles found in the “International Ethical Guidelines for Biomedical Research Involving Human Subjects”. These standards were developed from 1982 by the Council for International Organizations of Medical Sciences (CIOMS), in collaboration with the World Health Organization (WHO), and reflect the conditions and needs of biomedical research in developing countries, as well as the implications for multinational research in which they can be partners.

From a sanitary point of view, the complexity of the studies and the requirements of regulatory agencies led to the formulation of international standards to conduct clinical studies.

The most important international standard for Brazilian regulatory-sanitary standards is called 'Good Clinical Practice' (GCP-ICH), which provides standardized principles for the regulatory oversight of clinical trials in the world .

Since 1996 BCP has been recognized as the international quality reference for the vast majority of countries.

It should be noted that from the point of view of the BPC, Brazil is formally based on an adaptation of the GCP-ICH prepared by the Pan American Health Organization (PAHO), called the Document of the Americas.

Thus, the document aims to propose GCP guidelines that can serve as a foundation for regulatory agencies, as well as for researchers, ethics committees, universities and companies.

According to the parameters established by Normative Instruction 4 of 2009, ANVISA is responsible for BPC inspections in Brazil.

7 THE METHODOLOGICAL COURSE

In this section, I present the methodological path experienced to prepare this thesis paper. Firstly, it involves how I got the data. On the second section I describe how I organized and analyzed them.

7.1 How I got the data

I divided the methodological course in three paths, inspired in Villar (2019), which I adapted and named as follow: approximation, internalization and conection paths.

In a first verification of the research field, before the qualification phase of the project, and that I name of "approximation path", I carried out a survey of data available on websites that were directly or indirectly related to the clinical research segment. I obtained about 100 research sources by choosing the following indexers: "clinical research", "regulation of clinical research", "PLS 200/15" and "PL 7082/17".

I accessed news, opinion articles, interviews and lectures in written form, in audio and in videos, whose contents were transcribed, which enabled an "approach" or the phase of the beginning of the recognition of the controversies that took place around of the regulatory dynamics of clinical research in Brazil.

The approach work led me to the following websites and to the organizations that host them:

Table 3 Sites researched in the approach phase

Sites	**Organizations**
http://portal.anvisa.gov.br/	ANVISA - National Health Surveillance Agency
http://www.aliancapesquisaclinica.com.br/website/	ALLIANCE Clinical Research Brazil
https://abracro.org.br/	ABRACRO - Brazilian Association of Representative Organizations of Clinical Research
https://www.interfarma.org.br/	INTERFARMA – Association of the Pharmaceutical Industry of Research
https://www.camara.leg.br/	Chamber of Deputies
http://conselho.saude.gov.br/comissoes-cns/conep/	CNS - National Council of Health
http://www.focepbrasil.net.br/site/	FOCEP - Permanent Forum of Ethics Councils in Research

https://portal.fiocruz.br/	FIOCRUZ - Oswaldo Cruz Foundation
https://mrctcenter.org/	MRCT - Multi-Regional Clinical Trials
https://www12.senado.leg.br/hpsenado	Federal Senate
https://www.sbppc.org.br/home	SBPPC - Brazilian Society of Clinical Research Professionals

Source: Elaborated by the author.

It is important to observe that these sources fulfilled the objective of serving as a reference to the first insights regarding controversies and actants that would later integrate the object of the analyses.

The initial idea was to seek to understand the interactions between the several actors that surround clinical research, involving proponents, performers, participants, users and regulatory entities, all interconnected to what we call a meta-organizational reality.

In a phase that I call the "internalization path" of the research, I accessed the electronic environments of the Federal Senate and the Chamber of Deputies that record all the legislative activity of PLS 200/2015 and PL 7082/2017, involving the individualized work of each of their thematic commissions and collection of all documents of the process (project proposals, legislative reports, opinions, amendments, requirements, and complementary information).

The figures 13 and 14, below, illustrate the trajectory of the legislative process of PLS 200/2015[2] that passed through the Federal Senate between July 4, 2015 and March 13, 2017 when the project was sent to the Chamber of Deputies under number PL 7082/2017[3], whose activities began on March 13, 2017 without completion of the work until the closing date of this thesis.

The last movement of PL 7082/2017 occurred on August 11, 2021 when the a report by the Committee on Constitution, Justice and Citizenship (CCJC) of the Chamber of Deputies was presented, and that has not been approved by the Plenary yet.

Finally, I contacted the Legislative Advisory Office of the library of the Federal Senate and of the Chamber of Deputies through which I could access shorthand notes from the work meetings of the Legislative Commissions and of the Federal Senate. The information obtained

[2] https://www25.senado.leg.br/web/atividade/materias/-/materia/120560. Access in 05/10/2021.

[3] https://www.camara.leg.br/propostas-legislativas/2125189. Acesso em 05/10/2021.

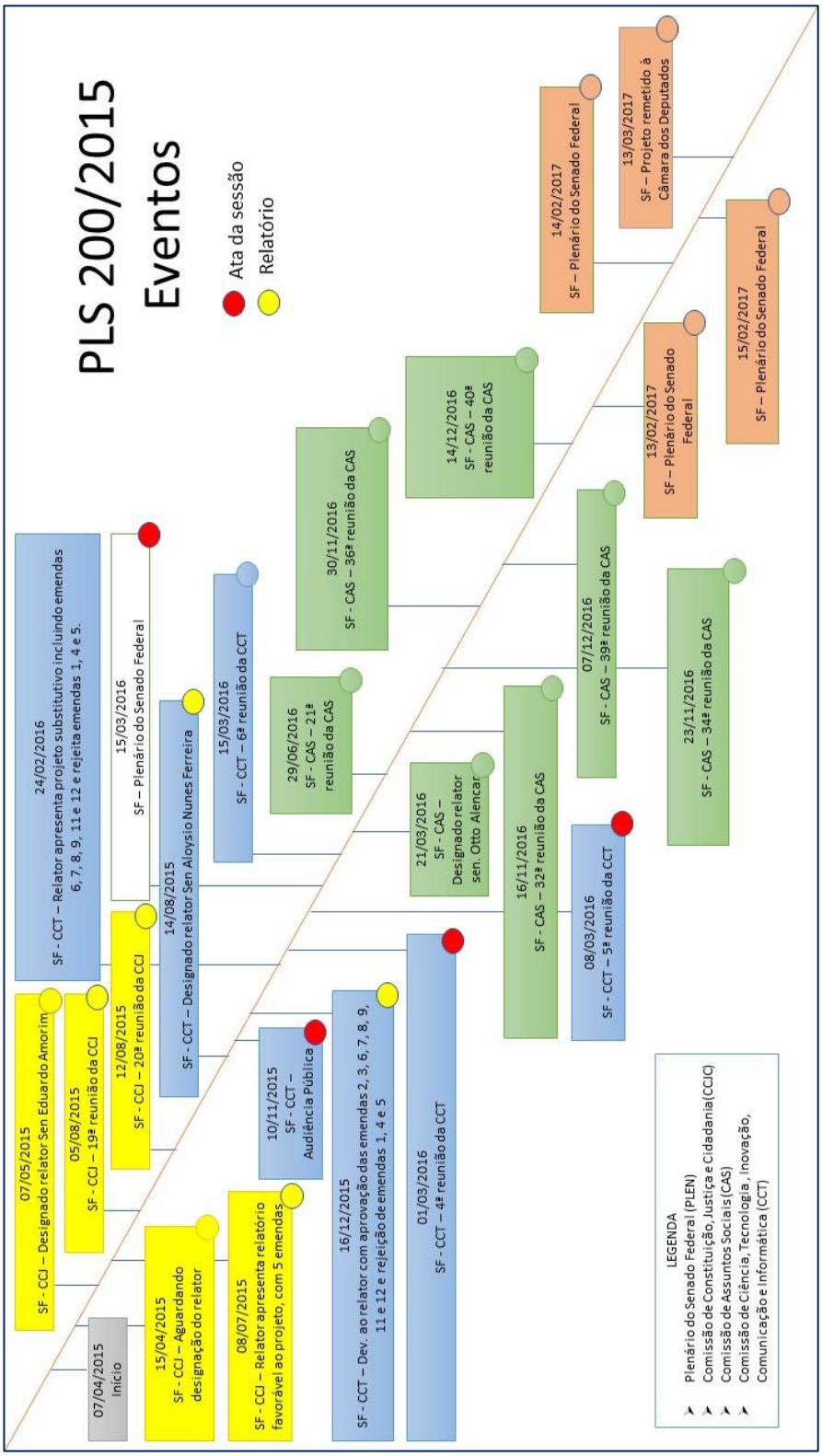
by the Senate came in written form, with literal transcription of all debates between congressmen and guests present at each legislative session and public hearings that took place.

In the case of PL7082/2017, in addition to the transcribed shorthand notes, the legislative sessions were also recorded in electronic media and all material was hosted on the Youtube video channel. Access links are available on the website of the Chamber of Deputies .

Finally, all normative acts produced by the National Research Ethics Commission (CONEP) and by the National Health Surveillance Agency (ANVISA) related to the regulation of clinical research produced during the processing period of the PLS 200/2015 and PL 7082/2017 were accessed.

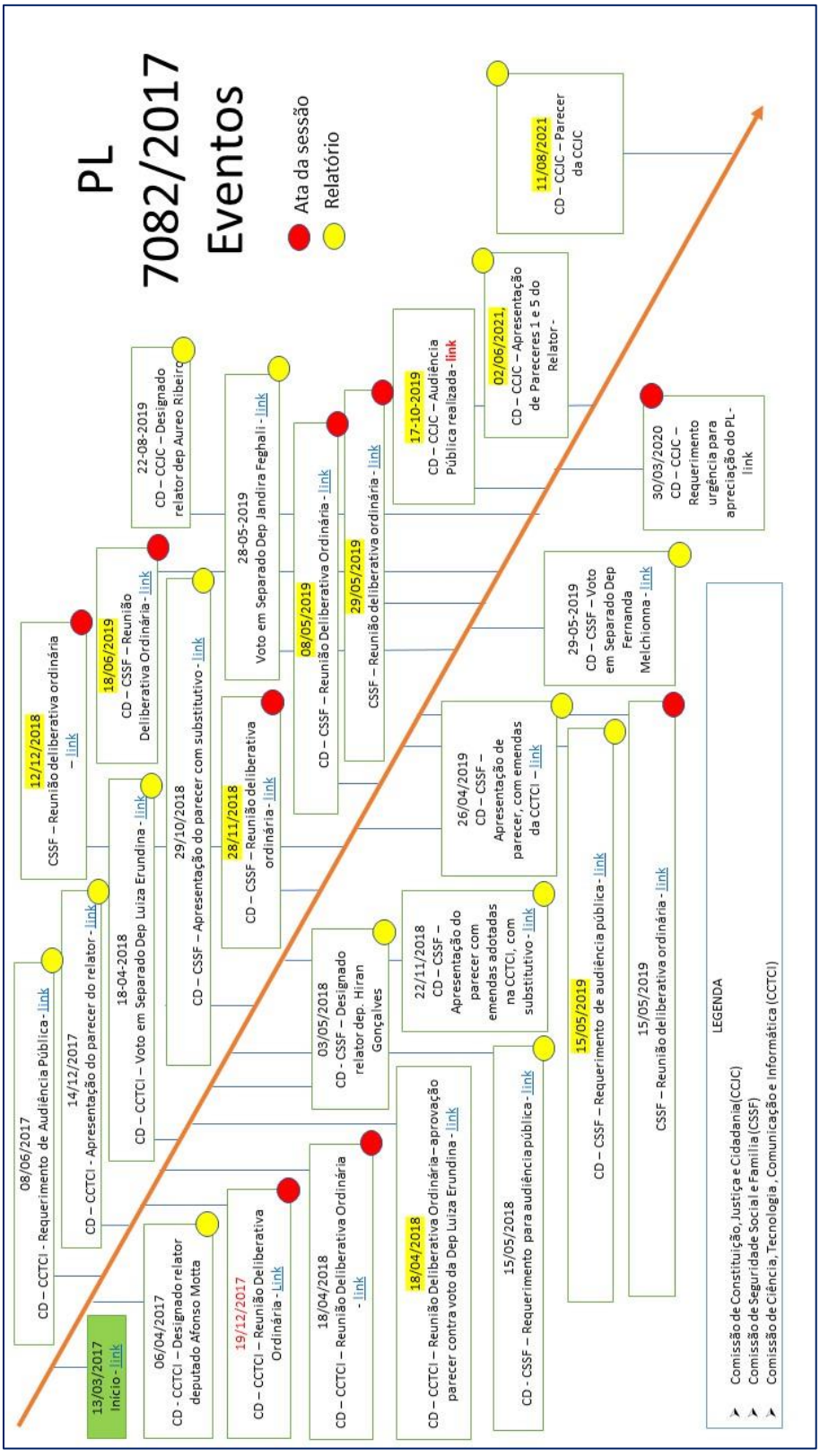
I obtained more than 200 documents – around 1500 pages examined –, involving documents and transcripts of interviews and lectures available on the websites surveyed, documents from legislative processes, shorthand notes from legislative sessions and public hearings, as well as normative acts produced by CONEP and by ANVISA

Figure 13 Proceedings of the Senate Bill (PLS) n. 200/2015



Source: Federal Senate, adapted by the author.

Figure 14 Proceedings of the Bill (PL) n. 7082/2017



Source: Chamber of Deputies, adapted by the author.

7.2 How I organized and analyzed the data

Here I describe what I called as “connection path”. Although in this report I am presenting a methodological process of research in a sequential way, the fact is that the phases of collection, organization and analysis were not pre-defined nor did they occur in a linear way.

I used Mitev's (2009) report, which highlighted the extreme difficulty and methodological uncertainties regarding ways to organize and analyze data in a research that uses ANT as an approach.

I also recalled the observation made by Latour (2007) that ANT allows the use of numerous research techniques upon the recommendation of an agnostic posture to the observer, who, devoid of any "frame", must simply travel through the field and report the what he sees. The research also assumed complete uncertainty about 'who' or 'what' would be acting (SAYES, 2014).

Several techniques have already been used in researches under ANT: the 'sociotechnical graph' (LATOUR, MAUGUIN, TELL, 1992); the 'semiotics' practice that were used by Latour (1984) in his seminal research (1984), and the “conversation analysis” (Simpson, 2007), among others.

Besides the techniques listed above, we were introduced to cartography that was widely disseminated in works based on ANT, and interested us mainly due to the contact we had with the European research project called MACOSPOL[4] – Mapping Controversies in Science and Technology for Politics, implemented by Latour in 2007, which consists of an European collaborative research project formed by researchers in Science, Technology and Society, with the objective of disseminating research resources that allow the sharing of controversies to scientists, professionals and citizens in general through a technological platform on the web,.

The MACOSPOL project stands out worldwide because it deals with complex issues by mapping the actions of human and non-human actants that participate in controversies, and it has in the researcher Tommaso Venturini, coordinator of the Media Laboratory of the University of Political Sciences in Paris, one of its main exponents.

According to Venturini (2010b), the cartography of controversies is the best way to observe the construction of social life, which is a technique widely adopted by Latour. Therefore, cartography of controversies was the technique adopted in this thesis.

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[4] MACOSPOL - *Mapping Controversies in Science and Technology for Politics.* Disponível em <http://www.mappingcontroversies.net> Access in 20/04/2020.

For Venturini (2010a), controversies that justify a cartographic study have the following characteristics: they involve action, they are emerging, restricted, well documented and openly discussed. The author also argues that the more technological the topic, the more effective the use of controversy cartography has been (VENTURINI, 2010a).

This thesis involves a subject that in our opinion fulfills the assumptions indicated by Venturini (2010a). Clinical research is a scientific-technological activity that has gained economic spectrum as it constitutes a segment of the pharmaceutical research industry, besides being involved in a relevant regulatory constraint that determines the competitiveness of that segment. Furthermore, the ethical, political, legal, economic and managerial aspects involved in this regulatory institutional dynamic make the controversies essentially complex, capable of being mapped through cartography.

In the cartography of controversies it is recommended that visibility be given to all points of view captured in the dynamic, taking into account their representativeness, influence of actants and interests inclusive of minority groups (VENTURINI, 2010b).

Venturini (2010b) also makes the following recommendations when mapping controversies: (a) 'adaptation', according to which the researcher should seek the greatest possible representation in the mapping of controversies in different sources of evidence; (b) 'redundancy', whereby there must be different representations through different specific maps, which, together will give a joint view that would surpass the partial views of each map; and in this sense, redundancy would consist of a way of stabilizing representations; (c) ‘flexibility’, which guarantees traceability between different translations of map representation.

Venturini (2010b) also refers to the possibility of reversibility or the possibility of scaling back its formalizations and trying other actant re-aggregations.

In this paper, through cartography, it would be important to guarantee the change from the individual's logic to the logic of a heterogeneous network. Thus, Latour (1988) gave the example of Louis Pasteur who did not exist as an individual but as a network composed of a laboratory, bacteria, computers, statistics, other computers etc.

A recent proposal to operationalize the cartography of controversies was made by Tureta and Clegg (2021), based on the work of Venturini (2010a; 2010b), Hartt et al (2014) and Hussenot (2014) that aims to develop a method for anti-history based on ANT.

These authors defined a process which unfolds in five relational and non-linear focal points, explained in the table below:

Table 4 Dispute Mapping Process

Step	Function	Description
Sampling	How to identify controversies	What types of controversies are at stake and what their connections are.
Scanning	How to map actors-networks	Follow the network of actors that is formed around controversies, looking for those whose participation made a difference in the actions of others, enabling to map who and what was involved in the controversies
Tracing	How to design the translation process	Seek to understand how network-actors relate, connect, disconnect and align, generating translations.
Labeling	How to analyze the policies of the actors-networks	Understand the relations and practices of power involved in the controversies, looking for what moves the actors to mobilize other actors, as well as what represses or silences them.
Describing	How to describe multiple realities and power relations	Identify excluded actors, bring up hidden events, and bring out the different possibilities of reality.

Source: Tureta; Clegg, 2021, adapted by the author

In this work it was necessary to emphasize the political interests that form and are formed by network-actors (MOL, 2001). We also took into consideration the possibility that different realities may coexist at the same time that they are excluding and divergent (MOL, 2002), which is made possible by the multiple character of reality that is not a fixed one and may always have been different, even through the influence of the researcher's observation has a performative effect on the narrative developed in this thesis report.

Thus, from the beginning to the temporary closure of the controversy it was essential to describe the representativeness, the influence of interests from divergent points of view, if a controversy was resolved, and if the result was legitimized and shared providing temporary stability.

Adopting the terminology proposed by Tureta and Clegg (2021), I identified the controversies ("sampling") by reading all collected documents and organizing them into "hierarchical trees" or "Poperian trees", which are graphical representations of controversies in which a plurality of issues are presented and make the debate complex (VENTURINI, 2010b; CERRETTO; DOMENICO, 2016).

This technique allows the dismemberment of arguments into hierarchical branches in the form of trees and meets the observation made by Venturini (2010b) that controversies cannot be reduced to a binary opposition of alternative points of view, as they involve multiple issues and situations that should be captured by the researcher.

There are different ways of representing the hierarchical trees of controversies, among which we highlight the technique of mental maps (VENTURINI, 2013), which allow us to visualize the position of each actor in their controversies, their relative importance, their relationships and their composition.

Considering that mental maps are representations of hierarchical trees, it would be necessary to understand the different hierarchical levels considered in this representation.

On the first level the 'issues' involved in a controversy are established. On the second level the 'positions' are placed, understood as the convergence of actants on one of the possibilities to solve the controversy. On the third level the 'arguments' that were used by the actants during the debates in favor of a given position are presented. The fourth level presents the human and non-human 'actants' involved in each argument (CERRETTO; DOMENICO, 2016).

As there is not a single controversy, but a chain of controversies, we follow the recommendation that one more hierarchical level be added to establish the 'relations' between them (VENTURINI, 2010b).

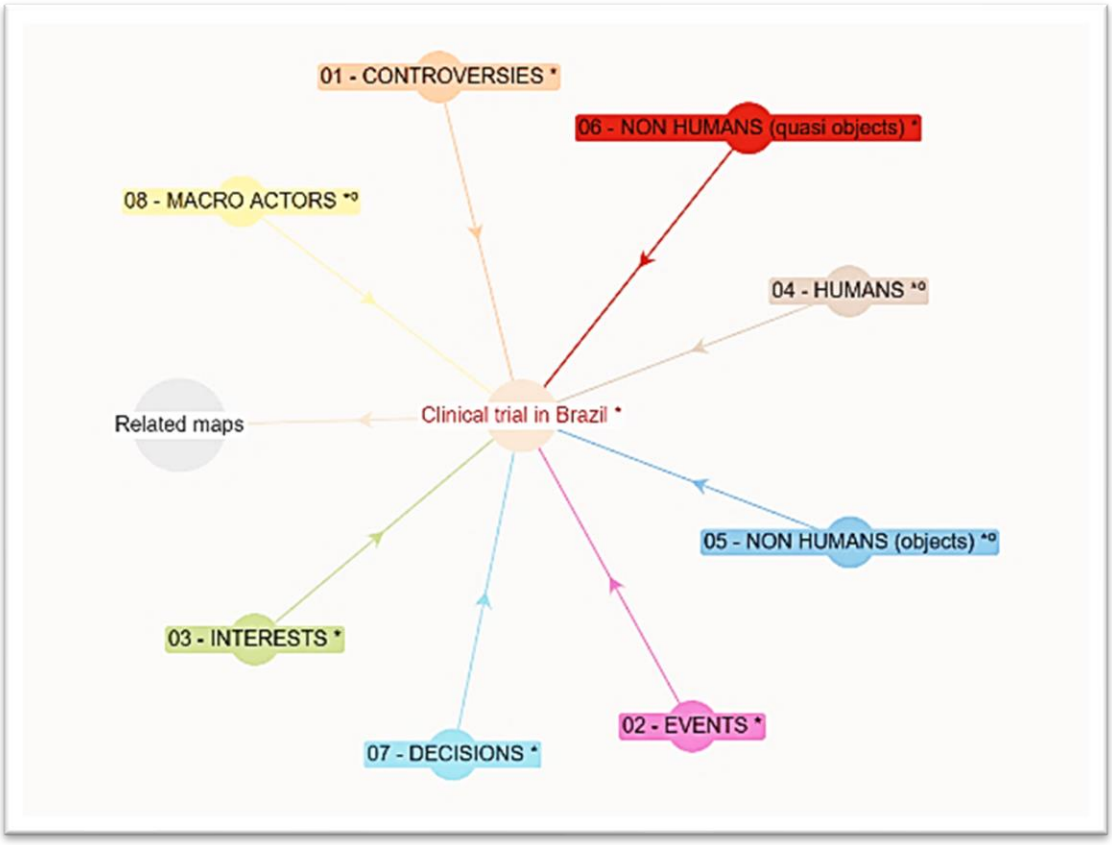
To operationalize the hierarchical trees we used the Debategraph[5] software, which is a web-based collaborative tool for visualizing ideas, focused on complex issues, enabling the creation and management of mind maps.

The map built for the operationalization[6] of the analyzes can be accessed remotely and an illustration of its basic structure can be seen in the image below:

[5] For more information about Debategraph, view the site: https://debategraph.org/home

[6] Access to the Clinical Trials Map of Controversies: https://debategraph.org/Stream.aspx?nID=661382&vt=ngraph&dc=focus

Figure 15 Map of Clinical Research controversies in Brazil



Source: The Author

Guided by the technique of cross coding and categorization (CORBIN; STRAUSS, 1990), which included both a priori and a posteriori coding, it was possible to carry out the "sampling" through the creation of a hierarchic tree containing the 'controversies', which hierarchically break down into (a) themes, (b) positions (c) favorable arguments and (d) arguments against each identified position.

From the identification of the controversies in their four levels listed above it was possible to extract the explicit and implicit 'interests' involved in the controversies.

Considering the focal point of sampling or scanning, the networks of actors involved in each of the controversies were identified, distinguishing between 'human actants', 'non-human (objects)', 'non-human (almost-objects)' and the 'institutional actors' or 'macro actors'.

All "events" that occurred during the processing of PLS 200/2015 and PL 7082/2017 were also described in chronological order. In each event place, date, a brief summary of the events, as well as the actants (humans and non-humans) involved were recorded.

Through "cross-link", in which each controversy is linked to the actants involved, it was possible to monitor the networks formed around each controversy, identifying the actors whose

participation made a difference in the action of others, making it possible to map who and what was involved in each controversy (the “scanning” process).

Also through "cross-link", (a) controversies are connected with (b) events and with (c) interests declared or implied by the networks formed by (d) actants, as well as with (e) decisions that are taken along the events, both from the intra-relational (legislative process) and inter-relational (which occurs in the meta-organizational universe) points of view. This seeks to design the translations that culminate in the closing of the black boxes (the “tracing” process).

In order to fulfill the "tracing" or design stage of the translation process, the 'decisions' taken during the course of the process were recorded, mainly represented by legislative deliberations, such as approval of amendments to the project and consolidation of versions of the project as it advanced. At the same time, the normative changes promoted by the CEP-CONEP system and by ANVISA were also registered, and reactions expressed by the other actants were from the legislative environment.

The a priori categories were “controversies”, “actants” (humans, objects, quasi-objects and macro-actors). The a posteriori categories were “events” and “decisions” and “interests”.

Abductive reasoning was used in this mapping. It consists in exploring the facts and allowing these facts to suggest a theorization, in back and forth movements between existing theoretical knowledge and observed phenomena.

Thus, in the “labeling” stage I sought to abductively understand the power relations and practices involved in controversies through the interactions of the various actants, paying special attention to the moments and spaces in which these interactions could change the course of action of the legislative process. The intention was to understand the production and maintenance of actor networks and how these actors are tied by reciprocal bonds and create or alter the reality in which they participate.

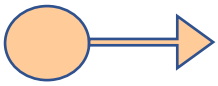
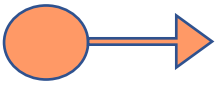
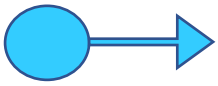
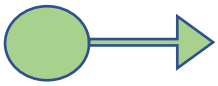
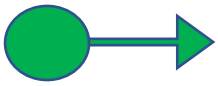
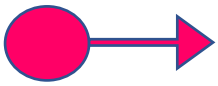
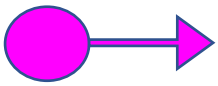
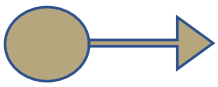
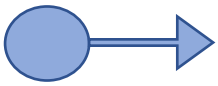
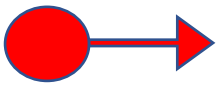
In this “labeling” focus they were also described as a group of entities, acting together and becoming a single voice, or in ANT's terminology, how an actor became scored.

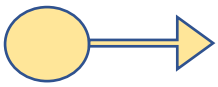
Finally, in “describing” I reassembled a narrative to tell a story about the regulatory process of clinical research, describing the case to exemplify the analysis from a procedural flow ontology, the observer's agnosticism, generalized symmetry and possibility of free association.

To identify the elements of the controversy map, the standard of colors recommended by the Debategraph was adopted, according to instructions of the command “what do the different colors and arrows mean?”, available in the tutorial of the “Debategraph” software. Please, see

below the key containing the meaning of each element and respective color of the controversy map:

Table 5 Structure of the controversy map used on this research

	Map	The map description identifies the subject that is being mapped
	Controversy (theme and sub-theme)	An issue arising within the subject matter of a map
	Position	A position taken in response to an issue
	Interest	Something that is valued by a person, group, institution or another type of stakeholder.
	Decision	A decision taken in response to an issue
	Support argument	An argument that supports a position or component thereof, or another argument.
	Opposing argument	An argument that opposes a position or component thereof, or another argument.
	Event	A meeting, workshop, conference or other type of event that is relevant here
	Human Actant	A person participating in the debate.
	Non Human (Object)	An object participating in the debate.
	Non Human (Quasi Object)	Another entity participating in the debate.

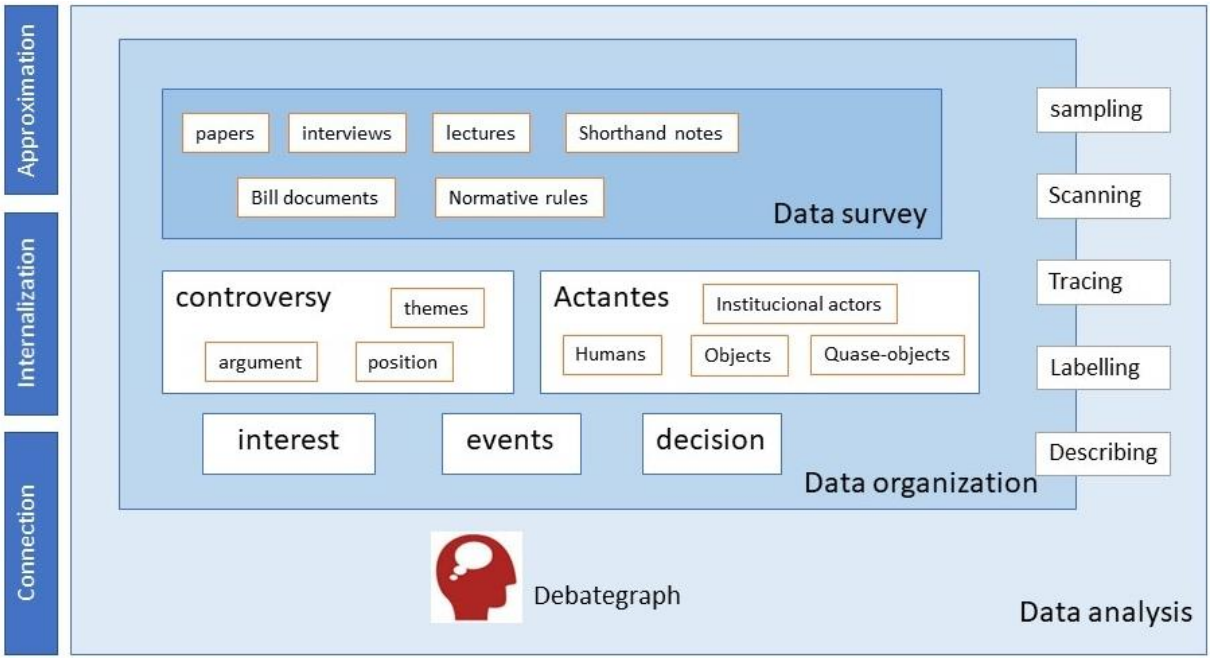
	Macro Actor	Human beings grouped and associated with non-humans

Source: Debategraph, adapted by the Author.

It is important to notice that the freedom employed to follow the paths of collecting and analyzing the empirical material of the research, opposing strictness of traditional methodologies allowed me flexibility in the process, as recommended by Czarniaswska (2006) in works based on ANT.

A summary of the methodological path can be described in the following figure:

Figure 16 Methodological path



Source: the author

Finally, some remarks are deemed necessary.

The first one is that the work of network actors does not cease. Thus, the eventual conversion of PL7082/2017 into a law that establishes the regulatory framework for the clinical research sector or the continuation of the progress of the project without having reached the objective established by its proponents at the moment this research is completed does not interfere with the search results.

We are not committed to initials or endings. The regulatory dynamics was studied with a retrospective, emergent and longitudinal focus (HUBER; VAN DE VEN, 1995), as it developed, in its fluid continuity line, in a time frame of the processing period of PLS 200/2015 converted into PL 7082/2017 until the closing of the thesis report.

Therefore, a linear or sequential logic in the development of clinical research is not being stated. Timelessness is immersed in the analysis in a spiral way, or according to Latour (2007), in a process in which the elements of the past made it possible to understand the present and the future.

The second remark is that generally research based on ANT has a micro analytical focus, which implies in the task of following the actants, observing closely their relations, actions, practices and methods used to carry out their associations (LATOUR , 2007; ALCADIPANI; DUARTE, 2016).

The posture recommended by Czarniaswska (2005) is that of an ethnographer, which constitutes the most suitable path for a direct experience where human and non-human agencies can be captured. Latour (2007) even states that the only way to understand the reality under construction is to follow it in its details.

In this sense, we recognize a limitation in our research because in the course of the dynamic that developed around the processing of a bill involving regulatory bodies, legislators, representatives of the pharmaceutical sector, not to mention the participating objects, artifacts and quasi-objects, their actions and associations are not spatially concentrated in a single location, but rather dispersed and occurring simultaneously. This makes it practically impossible to the researcher to monitor on the spot.

It was for this reason that the researcher's stance had a more historiographical than ethnographic focus.

The third remark is that the results of the research presentation must have a narrative approach that combines the hybrid between science and fiction. According to Law (2004), there would be in the ANT approach a license to deal with the chaos of realities, at the same time heterogeneous and procedural, by unusual or little-known ways in the social sciences (CZARNIASWKA, 2006; LAW, 1992; 1994; 1999a).

8 NARRATIVE DESCRIPTION OF THE CASE

In this chapter, the objective is to carry out a reconstruction of this narrative about the regulatory interfaces with the Brazilian clinical research activity.

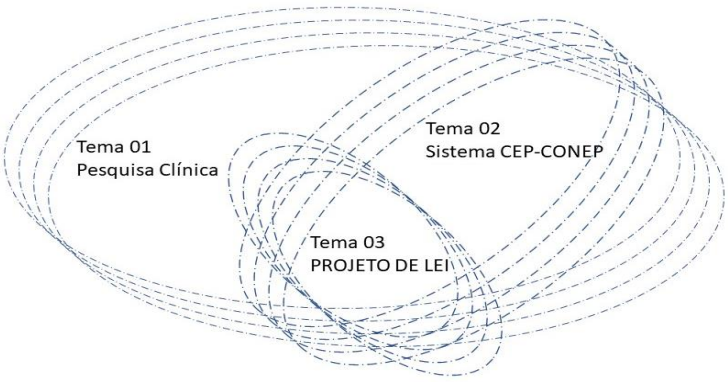
Through the narrative, guided by the cartography of the controversies identified in the research field, it is possible to illustrate a descriptive analysis guided by the ontology of process, the generalized symmetry and, above all, the performative mentality.

The narrative is not intended to record an exhaustive description of reality, but to produce a version based on choices (among the various possible ones) and whose performative effects are even in the creation of meaning that this author attributed to the facts from the contact he had with speeches of human actors, artifacts and hybrids throughout the construction of this thesis.

I also notice that reference to organizations, institutions and even human and non-human actors do not involve recognition of a substantive ontology, but the mere explanation of heterogeneous networks, whose procedural-relational nature must be recognized at all times in all the work. The entities will always be apparent structures and effects of networks formed by the action of multiple actants that sustain sociotechnical arrangements.

From the multiple ramifications and different traceable paths, I structured the reassembly of the story based on three narrative themes that helped me to understand the regulatory dynamics from a performative perspective: (a) clinical research, (b) the CEP/CONEP system and (c) the Bill of Law (PLS 200/2015 – PL 7082/2017).

Figure 17 Narrative themes of the case



Source: The Author

The narratives were built from the search to understand the relations that described the dynamics regarding (a) the meaning attributed to clinical research and the regulation involved

in it, (b) the controversies surrounding the ethical regulatory function (CEP-CONEP system) and (c) the legislative process that proposes a rearrangement of this regulatory dynamic, but also suffers performative effects in its construction.

Based on the analysis of these movements or translations of interests captured by the work of networks, in the following chapter our aim is to propose an analysis on the performativity of the interrelations of regulation (or internal dimensions of the arrangement), as well as on the performativity of intra-regulation relations (or in the dimensions of the interfaces with other actants) as a hybrid artifact or "agencement", which is in a constant recreation process.

8.1 Narrative 01: Clinical Research[7]

In a Latourian style, inspired by the first chapter of the work "Science in Action" (LATOUR, 1998), I present two scenes:

> **Scene 1**: Since the beginning of the 2000s, the promise of a cure for one of the most emblematic modern diseases, known as the "cancer pill"[8] has spread in Brazil and, behind it, an intense debate on the existential issue that it involves the trench between life, death and the means made available for widening that interval.
>
> Phosphoethanolamine was manufactured and distributed for about 20 years by the Brazilian chemist Gilberto Chierice, and gained fame as an effective medicine in fighting various types of cancer.[9]
>
> However, the distribution of the pill was prohibited by Brazilian regulatory bodies, as its development process was not subject to legal, ethical and sanitary standards, which are mandatory for any research activity in the country.
>
> The clamor of thousands of patients and their families, in favor of using the pill, led the Brazilian National Congress to enact Law 13.269/2016, which authorized the manufacture of the product without the control and registration of the Brazilian regulatory authorities.[10]
>
> However, to contain this attack, opponents of the pill filed a lawsuit before the Federal Supreme Court to make Law 13.269/2016 unconstitutional, so as to withdraw both the legal norm and the pill.
>
> The Federal Supreme Court considered the technical evidence of the substance's viability to fight cancer to be insufficient and, therefore the release of the pill would

[7]The map of theme 01 "Clinical Reasearch" can be accessed by the link: https://bityli.com/74QxrC

[8] RATINHO CHORA AO COBRAR DAS AUTORIDADES MEDICAMENTO PARA COMBATER O CÂNCER. Available at <https://www.hojeemdia.com.br/almanaque/ratinho-chora-ao-cobrar-das-autoridades-medicamento-para-combater-o-c%C3%A2ncer-1.356897>. Access on March 21, 2020.

[9]**LIVRO CONTA A DESCOBERTA DA FOSFOETANOLAMINA, A "PÍLULA DO CÂNCER". AVAILABLE AT <**http://www.ccet.ufscar.br/news/livro-conta-a-descoberta-da-fosfoetanolamina-a-pilula-do-cancer**>Access on Mar 21, 2020.**

[10]LEI SOBRE USO DA "PÍLULA DO CÂNCER" DIVIDE OPINIÕES DA CÂMARA, Available at https://www.camara.leg.br/noticias/486089-lei-sobre-uso-da-pilula-do-cancer-divide-opinioes-na-camara> Access on Mar 21,2020.

> be reckless for patients[11]. In fact, many patients, at the time abandoned the conventional treatment to adhere to the alternative one. Right versus doubt. Reason versus faith. Resources controlled against those who run outside the state's purview.
>
> **Scene 2**: Afonso Celso Haas, a sixty-year-old from Rio Grande do Sul, stricken by lung cancer and participating in a clinical research conducted by the Center for High Complexity in Oncology (CACON) of the Hospital de Caridade de Ijuí (HCI), contacted the office from Senator Ana Amélia, in Brasília to complain about the slowness caused by regulation in the process of developing new drugs in Brazil, which is a situation that harm thousands of cancer patients who are waiting for a cure[12].
>
> Moved, the senator called on doctors, researchers, representatives of the pharmaceutical industry and regulatory authorities to discuss the matter.
>
> Cancer, the fight for life, the rush and the criticized regulation brought together a terminal patient and a fearless senator so that they started a broad debate on the creation of a new regulatory framework for clinical research in the country, giving rise to the creation of Bill of the Senate number 200/2015 (PLS 200/2015)[13], submitted to the legislative process initiated in the Federal Senate, and which is currently being processed before the Chamber of Deputies under number 7082/2017[14] .

In 2015, an intense mobilization around the activities of clinical research was resumed in Brazil and a statement that associates its regulation with the delay in approving medicines that could save lives.

The phosphoethanolamine pill, Law 13269/2016 that regulates it, and the Federal Supreme Court that prohibits it, gave the initial contours to the problem of the regulation of clinical research that had been accused as one of those responsible for the death of cancer patients.

Network "Afonso Haas+cancer+Cancor+HCI" joins network "Ana Amélia+Federal Senate" to start an activity to reconfigure the artifact "regulation of clinical research" and the relations associated to them.

We chose to map some of the controversies that we believe were guiding this process and therefore we listed some points of discussion, which occurred during the legislative activity that took place during the processing of PLS 200/2015-PL7082/2017, involving not only the rhetorical resources of parliamentarians during the legislative sessions, but also of several actants, representatives of sponsors, scientists, participants, ethics committees and other regulatory bodies that in public hearings participated decisively in the debates.

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[11]SUPREMO TRIBUNAL FEDERAL. Available at: <http://www.stf.jus.br/arquivo/cms/noticiaNoticiaStf/anexo/adi5501MMA.pdf>. Access on Mar 21, 2020.

[12] SEMINÁRIO DEBATE PROJETO DE ANA AMÉLI PARA AGILIZAR LIBERAÇÃO DE PESQUISAS CLÍNICAS. Available at <https://www12.senado.leg.br/noticias/materias/2015/04/15/seminario-debate-projeto-de-ana-amelia-para-agilizar-liberacao-de-pesquisas-clinicas.>. Access on Mar 21, 2020.

[13] To access the full text of PLS 200/2015, please see <https://legis.senado.leg.br/sdleg-getter/documento?dm=4584489&ts=1567526423918&disposition=inline>. Access on Apr 30, 2020.

[14] To access the full text of PLS 200/2015, please see <https://www.camara.leg.br/proposicoesWeb/prop_mostrarintegra;jsessionid=E460327AB966D9BA799567B282255D39.proposicoesWebExterno2?codteor=1793270&filename=PL+7082/2017>. Access on April 30, 2020.

We also collate the non-human agency whose wills are represented by the speeches of human actors as they begin to assume the voice of the heterogeneous network that mobilizes them (LATOUR, 2007).

a) The delay in clinical research (CT01.01)[15]

The debate on the regulation of clinical research starts enthusiastically in the Constitution and Justice Committee of the Federal Senate. The networks defended by the Senators are eager to release medications and cancer is the actant that most afflicts them.

> "If you had cancer, what would you do? I would even eat dirt. (...) The right to life is in the Constitution (...) and we have to do something for life. We have to shorten time, we have to make it easier. (Senator Ivo Cassol, CT0101 P01 b4, on 11/10/2015)

Delay affects the poorer.

> "My grandson needed medication that was not authorized to use. We imported 4 ampoules. And what about the boy who was born in *Climério*?" (Senator Walter Pinheiro, CT0101 P01 b6, on 11/10/2015)
>
> "Even the president had cancer and was cured with a drug that didn't bear authorization then." (Senator Ivo Cassol, CT0101 P01 b5, on 11/10/2015).

Delay scares away the researchers who are leaving the country.

> Cláudio Juazeiro has been a researcher for a long time at the Novartis Laboratory. This young man left Salvador at the age of 18; today he is one of the greatest researchers in the world. We have been trying to repatriate him since 2007, but we can't afford it. He says: "What I'm going to do in Germany currently I'm not in the least able to do in Salvador". (Senator Walter Pinheiro, CT0101 P01 c, on 11/10/2015)

Delay harms the generation of industrial property.

> "An anticancer plant was discovered at the Federal University of Ceará, but bureaucracy made the research to be conducted in the USA". (Senator Simone Tebet, CT0101 P01 to ob002, on 08/05/2015).

The reaction to the explosive rhetoric of critics of regulation is parsimonious but blunt.

The networks against PLS 200/2015, led by CONEP, follow the Latourian maxim of minimizing controversy with the following tactic: "any effort to reduce deadlines will have our support" (Jorge Venâncio, CT0101 P01 f, on 11/10/ 2015). It is as if they were saying that "we all want the same things" (LATOUR, 1998, p. 312) and we are against "delay".

However, the actors-networks triggered to flaunt the "hurry" were silenced by the following data:

[15]To access the map of controversies CT0101 use link: https://bityli.com/74QxrC

> “Response time of CONEP decreased from 10-11 months to 48 days. This idea that there are still projects taking a year or a year and a half is completely unrealistic at the moment.” (Jorge Venâncio, CONEP, CT0101 P01 d, on 11/10/2015).

> “We recently received for analysis the phase 3 proposal of the research of the vaccine against dengue from the Butantã Institute. And we managed to approve the research in 38 days with two procedures: 17 days in the first procedure and 21 days in the second one, which is 38 days”. (Jorge Venâncio, CONEP, CT0101 P01 d3, on 11/10/2015).

And more information has been listed, in a universe where numbers are invoked as easily as they are refuted.

> “We recognize the efforts of CONEP to reduce the time it takes to analyze the research protocol, but let us point out that what actually decreased was the first opinion. Unfortunately, this first opinion has been coming with numerous pending issues. Sometimes there are more than 40 pending issues. (Fábio André Franke, ALIANÇA BRASIL, CT0101P01 d2, on 11/10/2015)

In short: what good is the decrease in time response of CONEP if the levels of demand remain the same, and as a practical result clinical research fails to advance? Haste is now associated with bureaucracy.

Cancer, the prospect of death, injustice to the poor, the flight of talent and the loss of intellectual capital are effects caused by the delay in clinical research that "slips" thanks to "bureaucracy", a recurrent actant vocalized by human actors, and whose agency triggers all the collocated wrongdoings.

After all, "researching in Brazil is almost prohibitive" (CT0101 P02 b), the existing system is "inefficient, anachronistic, and marked by serious distortions" (CT0101 P02 a), besides “scaring industry away" (CT0101 P02 c) and "harming the scientist" (CT0101 P02 d):

> “There is no shortage of professionals, there is no shortage of researchers; there is an excess of bureaucracy! So it's really time for us to end this ailment and this suffering, and bring our researchers who are abroad and encourage them even more. This country has a way, and for sure this Commission sets a good example in Brazil at this moment. (Senator Eduardo Amorim, CT0101 P01 h, on 03/15/2016).

Regulation, as a socio-technical artifact, was constituted as a starting point, by relations with slowness and bureaucracy, and with the propagating effect of disease, generator of death, promoter of injustice, scaring away talent and reducing wealth.

The “hurry” that would justify the deconstruction of the regulation for fastest clinical research shifted to the search for the speed of the PLS 200/2015 itself.

If data war alone was not enough to contain and deconstruct the regulation, in the case of the search for the speed of PLS 200/2025 new actants proved capable of such purposes: the Internal Regulations of the Federal Senate and the Chamber of Deputies.

They provide requests for "views" that can be requested by any parliamentarian and which suspend the course of a bill for the time determined by the president of a legislative committee.

As the requests for a view were required, thus creating even greater delays in the processing of PL 200/2015, haste, cancer and death were invoked once more:

> "(...) I want to take advantage of the opportunity, since Senator Randolfe Rodrigues asked for a view, to make it collective, having in view the urgency of the assessment and approval of this matter because while we are here debating on the issue of releasing phosphoethanolamine with less bureaucracy after everything that is available to society has been used, I'm sorry to say that the cancer patient can no longer wait, as this patient has already undergone chemotherapy that not only fights dead cells but also brings significant harm to health. (Senator Ivo Cassol, CT0101 P01 g, on 03/01/2016).

> "A person with cancer cannot wait – cannot wait! I am deeply sorry. Other people of the same age and with other types of cancer did not have the same privilege [as Adolfo Hass] of having entered the research. What happened? They died! They died because they did not have access to clinical research. And that's what we are in a way doing when we're slow to vote a process of this nature: letting people who have cancer die, waiting, at the door of hope, for research that can give them survival. And, Senator Vanessa, I'm sorry about this request for a review because we're going to delay a matter of this nature for one more week. (Senator Ana Amélia, CT0101 P01 i, on 11/23/2016).

Unsuccessfully. The regimental right of view quickly overtook cancer and death. And, with the "view", the technical qualifications of the network 'senator-pharmacist' were associated, as well as the political rights of the network 'pharmaceutical-citizen'.

> "I want to repel all the manifestations that tried, deliberately or not, to address to concluding that my attitude is or would be hinder the approval of this project. So, I immediately reject any remark in this regard. And I do not speak only as a Senator; I also speak as a health professional, I speak as a pharmacist and I also speak as a Brazilian citizen who is as sensitive to the need for advancing research in Brazil as any other citizen who knows our reality, Mr. President. I know it is an extremely controversial project not only here but in the academic environment as well, very controversial – very controversial! (Senator Vanessa Grazziotin, CT0101 P01 j, on 11-23-2016).

Several views were granted and PLS200/2015, converted into PL 7082/2017, has been in process for years with no prospect of completion. Where was the rush anyway?

> "You see, in the civilized world a research is registered in 60 days – 60 days! And this law is here in the Congress, in the Federal Senate, being processed for more than two years. (Senator Ana Amélia, CT0101 P01, l, on 02/13/2017).

And if the rush did not move parliamentarians to speed up the processing of PLS200/2015, the same cannot be said of the infra-legal revisions of CONEP itself, as deadlines have gradually been reduced to the point where Brazilian processing times have become shorter than those practiced in the United States.

> "The processing time at CONEP was the main problem we faced as soon as we took over the coordination of the commission, 5 and a half years ago, in mid-2013 we had a very high processing time. When we arrived we were doing 75 reviews/month and we had 830 awaiting analysis. The length was this: 330 days. This time has dropped and, as of May 2016, it is below 30 days. Here we can see the current situation: from May 2016 until now the system is stable, and the period is below 30 days. It's varying 2 days more, 2 days less, but all the time it's under 30 days. It is important to notice

> that we have frequently approved research in Brazil faster than in the United States. (Venâncio, CONEP, CT0101 P01 m, on 12-06-2018).

And finally, the promoters of PLS 200/2015 celebrate the performativity of the initiative to state that the improvement of regulation has advanced despite all the obstacles to the creation of the legal framework for regulation .

> When we first discussed this issue there was a movement, as recognized here by Dr. Paulo Hoff. Institutions began to move. (Senator Ana Amélia, CT0206 P01 b, on 11/10/2015)

b) Access to clinical research (CT01.02)[16]

Due to its delay and bureaucracy the current regulation of clinical research has also been accused of hindering participants' access to the benefits of experimental treatments.

> "We keep waiting for more than one year to include Brazilian patients in research protocols. And, in general, when this approval is granted, these studies have already closed participation because they are global and multi-institutional across the world. Patients who have a potential to receive treatment, especially for serious illnesses, do not request them, and end up missing this opportunity. Our hands are tied up and we are unable to offer anything that can be meaningful and represent hope for the patient. (Fábio Franke, Aliança, CT0102 P01, on 11/10/2015).

And the difficulty in accessing experimental treatments, especially in cases of serious and rare diseases, leads patients to seek alternative, unsafe and uncontrolled treatments:

> "Non-access to experimental treatments has led people to undergo alternative treatments. We don't want people to fall into the trap of undergoing some alternative treatments in their desperation to find something. (Fábio Franke, Aliança, CT0102 P01 b, on 11/10/2015).

This problem does not happen only in Brazil. In other countries, difficulty in accessing clinical research has resulted in thousands of deaths:

> "In a single study in the United States and the United Kingdom, it is estimated that more than ten thousand unnecessary deaths occurred, and are directly linked to the delay in the recruitment of research patients" (ALIANÇA - Fabio Andre Franke CT0101 P01 b, on 11/10/2015)

The arguments in favor of the bill also emphasize the benefits of promoting a favorable environment for the development of clinical research in the country:

> "[Clinical research] allows many patients to have a chance of treatment they would not have otherwise; it offers the possibility of treatments that are not available yet, that are under development, that are very important, especially to treat diseases that have no treatment yet or to establish treatments that can mean an improvement for the patient. (Raphael Sanches, ANVISA, CT0102 P01 d, on 12/06/2018).

[16]To access the map of controversies CT0102 use the link: https://bityli.com/74QxrC

Besides benefiting patients, benefits to the SUS were pointed out, as the expansion of clinical research would reduce the burden of a collapsed system, once such treatments would be funded by research sponsors:

> Yesterday we did a “blue November” [campaign] per my request. What for? To prevent and draw attention to prostate cancer. And do you know what happened in the public hearing broadcast throughout Brazil? A retired public servant from Betim, Minas Gerais called to say the following: "Senator Ana Amélia, it's no use campaigning for prevention. For 18 years, I've been asking a public system to undergo a prostate exam. 18 years! And I haven’t been successful so far. (Senator Ana Amélia, CT0102 P01 c, on 11/10/2015).
>
> The citizen who is in the SUS queue often thinks that research is a condition for him to continue having access to public health in our country. (Claudio Araujo, UFBA, CT0101 P01 b1, on 11/10/2015)
>
> “In any bill we have to see what benefits it will bring to patients, to the community in general and to the Government. What is the effect on the Government of the fact that phase two of this research was done here, not in the United States or in other countries? This research has already recruited 20 patients for phase two. These 20 patients currently cost the Ministry of Health around 20 million per year in treatment. And in phase three 30 patients will be recruited that cost 30 million. So, see how much savings this will bring. (Antoine Suheil Daher, Hunter Institute, CT0102 P01 e, on 12/06/2018)

The reasons for the development of the clinical research segment increase when the benefits are related to the technological challenges for the progress of medicine.

> “When I talk about rare diseases, I must say that the future of medicine is towards genetic diseases, with the technology behind these genetic diseases, with DNA mapping, neuronal mapping, cell therapies, gene therapies. That's the future.
>
> I joked with Dr. Flávia saying that the doctor who doesn't understand about genetics in 10 years' time might work as an Uber driver.
>
> If we really want to invest in first world medicine, we have to invest in new technologies. We have to bring all the research from the world here to Brazil to train the centers, save our patients, save Brazil. In healthcare, in the next 5 to 10 years, the biggest challenge will be to understand these new therapies. (Antoine Suheil Daher, Hunter Institute, CT0102 P01 f, on 12/06/2018).

c) Consent (CT01.03[17]) and ethical conflicts in clinical research (CT01.07[18])

If clinical research is so favorable to the population, to the country and to scientific progress, then why hinder its advancement?

And 'research' itself, as an actant, is the key to understand that all these benefits take their toll, as research involves discoveries, experimentation and the possibility of not finding what

[17]To access the map of controversies CT0103 use the link: https://bityli.com/74QxrC
[18]To access the map of controversies CT0107 use the link: https://bityli.com/74QxrC

one is looking for. There are also unanticipated and uncontrolled adverse effects that must be avoided or mitigated, especially when research participants are human beings.

The social-technical networks of regulation and clinical research have enlisted new allies, expressing the ambivalence of the artifact: on the one hand, regulation, which promoted death did not contain cancer and was bureaucratic, now saves lives. On the other hand, clinical research, which until then generated jobs, supported the SUS and was responsible for the progress of science, now produces deaths as well.

If both clinical research and regulation can save and kill, the benchmark to find a balance in this antagonism becomes the consent of research participants, a new actant, which must be free and clear.

An important ally of regulation was the Indian case, which followed the same steps (of deregulation) recommended in PLS 200/2015, thus making the rules for controlling clinical research more flexible. However, the results of the experiment were catastrophic: 370 deaths in clinical studies in 2 years. Between 2005 and 2012, 2600 patients died. The Supreme Court of India then decided to suspend research in the country until regulation was more adequate (Jorge Venâncio, CT0105, on 11/10/2015).

The newspaper "*The Times of India*" is enlisted to endorse CONEP by reporting clinical research performed with young girls, without parental consent, involving adverse effects of HPV vaccination tests. Follows a text (actant) reproduced by Jorge Venâncio at the public hearing of the Federal Senate on 11/10/2015:

> "Those girls' parents weren't even aware that they were part of the research and were given an experimental vaccine. Perhaps the independent Ethics Committees thought that vaccination, which was part of a Phase 4 clinical trial, was not a substantial risk and that it was therefore enough to get the consent of the owner of the inn where they were staying rather than getting in touch with the girls' parents who could be illiterate and therefore unable to understand the nature of the research. Or maybe they thought that approaching parents and asking for their consent for the HPV vaccine could be culturally inappropriate and problematic as it involved sexual activity among adolescent females, which is a taboo in India, what would mean that the parents would not be willing to give such consent" (excerpt from the article published in the Times of India, reproduced by Jorge Venâncio, CONEP, CT0103 P01 b, on 11/10/2015).

At the same time that Indian deregulation is allied *a contrario sensu* to the defense of Brazilian regulation, an anti-history is rescued to recall the origins of ethical legislation and its function to protect participants' freedom of consent in clinical research:

> This need came from certain abuses that took place during World War II. There was a whole international debate about these terrible experiences, and there emerged several norms whose main concern is to protect research subjects, especially regarding their autonomy and the need to get the subject's free and informed consent to participate in the research. (Fernanda Sobral, SBPC, CT0103 - P01, on 11/10/2015).

As the difference between drug and poison lays in the dose that is given, discussion here arises once about whether the consent of clinical research is an act of the participant, who expresses himself freely, or whether the vulnerable and unable to discern participant has his or her freedom compromised or suppressed.

The clinical research of the “cure of diseases” and “progress” combined with the artifact of “regulation that kills” will remain with the consent as an individual act of the participant.

Clinical research regarding the “Indian experience” that took place in the “second world war”, allied to the “regulation that saves lives”, will remain with the mitigated consent, where not even the participant alone can decide. It is the dispute between “freedom” and “security”.

From the point of view of ‘freedom’, regulation cannot be conceived to protect participants beyond what they wish to be protected. The final word belongs to the one who is protected and not otherwise.

> It's as if we watched our house so much, putting up a security system, putting up lookouts, putting up doormen, that not even the owner of the house can get inside it. It is so guarded, so surrounded, that we deny our Brazilian patients access to treatments that could mean better life expectancy and a dignified treatment for their disease. Fabio Franke, ALIANÇA BRASIL, CT0107 P02 a, on 11/10/2015.

And, by the way, whoever is in the middle of a fire (or has a terminal illness) will do anything to survive.

> “Joelma building” was on fire. Those people didn't throw themselves out of the building because they wanted to, but because it was the only alternative they had to save their lives. If I'm going to burn to death, I might think, "I'm going to throw myself off the twentieth floor, and maybe something will happen, and I'll end up surviving this tragedy." (Senator Omar Aziz, CT01.07 P01 a, on 11/10/2015)
>
> If a person has cancer or a terminal illness, that is a tragedy for their life. Any Brazilian citizen would choose to take tests to try to survive. I think that one should never deny someone an opportunity to survive (Senator Omar Aziz, CT0107 P01 b, on 11/10/2015)

However, from the point of view of ‘security’, it is precisely despair that suppresses free and informed consent from people, requiring them to be protected even from themselves.

> The first question that I think is important to be clearly defined is the following: what is the function of an ethical regulation system, which exists in Brazil and throughout the world? The function of an ethical regulation system is to protect the vulnerable side that exists when research takes place. I refer to the research participant.
>
> Note that when called to participate in a research, the participant is often desperate. Imagine a person who has just been diagnosed with cancer, for example: when the person is called to participate in the research, he or she is fighting for life. The last concern the person will have is whether his or her rights are being respected in details etc.
>
> It is precisely because of this situation, of this imbalance, that a system of ethical regulation was created around the world (Jorge Venâncio, CONEP, CT 0107 P01 c, on 12/06/2018).

It is not just about mitigating the right to free consent of clinical research participants, but to reconcile conflicting interests of those who want a cure and those who want to profit from the cure despite the lives that are lost along the way. :

> "Sometimes, eager to solve the problem, we have the fox taking care of the hen house. If we don't pay attention to details, especially those regarding private autonomy, manifestation of the will of all sectors, we do run the risk of having the fox taking care of the hen house. (Claudio Roberto Camperlingo Araujo, UFBA, CT0103 P01 c, on 11/10/2015).

Conflict between freedom and security shifts to an apparent dilemma between "protecting the participants" or "taking care of the patients". It's as if we were faced with "Sophie's choice"[19]. Would it be acceptable to sacrifice participants in order to save patients? Or to protect participants will we live as much as necessary with the deaths of patients? (CT01.07 P02).

The dilemma is rejected:

> It is perfectly possible to carry out a research respecting the rights of the participants and having clear humanitarian criteria, so that things are kept in a good standard, as we evolved after Resolution No. 96 that created Conep in 1996 (Jorge Venancio, CONEP, CT0107 P02 b, on 11/10/2015).

But "hurry" reminds regulation that the reasonableness of time for clinical research is also an ethical precept to be protected, inclusive by the very regulation.

> There is need for ethical control and it is necessary to have time to do this. All these steps guaranteed by the CEP/CONEP System cannot go against the necessary time to evaluate each protocol in an ethical way. (Rodrigo Stabelli, FIOCRUZ, CT0107 P03 a, on 11/10/2015).

The ambivalence of artifacts that fight for a definition of regulation seems to recalcitrate. Time and ethics need to come to an agreement.

d) Brazilian participation in global clinical research (CT01.04)[20]

When the delay in clinical research was attributed to regulatory bureaucracy, another controversy arose: the relevance of the Brazilian research segment if compared to other countries. And here, the 'endorsement' tactic was reinforced by the 'stacking' technique. A clash of numbers is established around the statements:

(A) Brazilian clinical research is (is not) relevant in the world

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[19] "Sophie's Choice" is centered on a scene in Auschwitz where Sophie has just arrived with her ten-year old son, her seven-year old daughter and a sadistic doctor, presumably Doctor Mengele, who tells her she can only bring one of her children; one will be allowed to live while the other is to be killed. In: https://www.urbandictionary.com/define.php?term=Sophie%27s%20choice. Accessed on 22/11/2021.

[20] To access the map of controversies CT0104 use link https://bityli.com/74QxrC

(B) Brazilian clinical research is on the rise (or declining)

The small participation of Brazilian clinical research (when compared to the US) is challenged by comparing it to Japan, a powerful country. This time Brazil wins:

> "Brazil has more research than Japan, Russia and India. So, we are not in such a negative situation (Jorge Venâncio, CT0104 P01 b, on 11/10/2015).

In the case where Russia is cited, new actants are enlisted to weaken the endorsement:

> "Russia is not a model to be mentioned here. Russia is a model for doping athletes to win a competition! We have to compare comparable things! (Senator Ana Amélia, CT0104 P01 b1, on 11/10/2015).

Comparability criteria are changed to attest to the relevance of Brazilian participation in clinical research, this time considering the universe of South America:

> Brazil accounts for roughly half of the clinical research in South America, but when we look at the research numbers, we are far behind Europe, the United States, Canada and other countries that are about the same level of our country. We are certainly not at the bottom, but there is a very long way to go. (Paulo Marcelo Hoff, ICESP, CT01.04 P01 d, 11/10/2015).

In any case, the international recognition of Brazilian clinical research is invoked once again (CT0104 P01 g) to raise a new controversy: is this recognition gaining or losing ground?

The network "Jorge Venâncio+CONEP", states that "research in Brazil is already increasing. We are not with research that stagnant" (CT0104 P01 c, on 11/10/2015), but for the network "Paulo Hoff+ICESP":

> "We are having a reduction in the number of projects. These are the projects submitted by multinational pharmaceutical companies to the Cancer Institute in recent years. You can see that the linear curve shows that we are having a reduction in the research offer being offered to our institution. I cannot tell for the whole country, but regarding supply interest in Brazil has dropped. (CT01.04 P01 a, on 11/10/2015).

Finally, upon so many divergences of data and interpretations in the attempt to endorse the debated propositions a stacking was finally preformed. CONEP presented the data collected from the website www.clinicaltrials.gov elaborated by the "National Institute of Health" (NIH), showing that 40% of the world surveys are within the United States, 28% in Europe and 32% in the rest of the world:

> "Let's look at the picture from the rest of the world. Brazil is in the fifth place; Canada in the first; China in the second; Korea; Israel; Brazil is in the same rank as Israel; we have recently surpassed Australia, we are ahead of Japan, the third largest economy in the world, and we are ahead of the other BRICS; Russia; India; ahead of Mexico; in Africa, the first country is Egypt and ahead of Argentina (Jorge Venâncio, CT0105 P01 a, on 12-06-2018).

The criticism of the meager Brazilian participation in clinical research is then deconstructed, through the establishment of the 'capturing' technique, which consists of ordering the easiest arguments and then listing the most difficult ones.

‘Jorge Venancio+CONEP´’ recognizes the need for progress (“I want what you want”), and opens two new arguments to contain the criticism of the low relevance of Brazilian clinical research: (a) the position we have reached represents the result of decades of effort, which cannot be ignored; (b) regardless of where we are, what matters is whether we are moving forward or taking steps backward.

> “So what comment would I like to make? Don't we have things to move forward? Of course we do. We have a lot to go forward, but thinking that we are at the end of the line... From time to time, we hear that there are only 2% of the world's research in Brazil; 2.3% is the reality. But the population of Brazil is 3% of the world population. So what does ‘2.3%’ meant? It means that we need to improve, but we are not at the end of the world; that is not the situation. Saying that in Brazil only paper is written seems to me an unfair disqualification of researchers and our research centers. Of course we have to move forward, but the main basis for moving forward is what we have already built in order to move forward. If we don't respect each other, who will respect us? The principle for walking, going ahead developing has to be to respect each other in the first place. Therefore, the question I ask here is *"What would Brazil gain by evaluating its Research Centers and the work of its researchers more negatively than the analysis carried out by the US government itself and published on its official website?"* This is the question I would like that remained for reflection (Jorge Venâncio, CT0105 P01 b, on 12-06-2018).

The efforts for deregulation (as in India) would constitute the setback, since the greater participation of international laboratories in Brazilian research would be “badly negotiated” in exchange for the withdrawal of the participants’ rights and all this without guarantees that such agreement would even be fulfilled.

> “There is a certain naiveté in the negotiation tactics. First, we granted the rights of our patients who are participating in the surveys in order to gain goodwill and thus place a greater set of surveys in the country (Jorge Venâncio, CT0104 P01 f, on 11/10 /2015).

e) The need for a law to regulate clinical research (CT01.06)[21]

Parallel to the unbundling of the relations that support clinical research and its regulation the controversy that most interferes in the dispute that appears in the works of PLS 200/2015 (and PL 7082/2017) arises: the issue regarding whether a law is really necessary for clinic research to improve in the country.

In defense of the law, rhetoric took on a characteristic of ‘stylization’ (which is a protection against the future through the repetition of the proposition to the point it detaches from its author): there is a "legislative gap” in clinical research" (CT0106 P01), there is a lack of “legal validity” (CT0106 P01 a) to its regulation; “the system is fragile” (CT0106 P01 a);

[21]To access the map of controversies CT01.06 use link: https://bityli.com/74QxrC

“we have laws for animals but not for people (CT0106 P01 b); “our rights must be enshrined by law and not by resolutions” (CT0106 P01 c); “without law we do not know how long the research will last” (CT0106 P01 d); “CONEP resolutions are authoritarian” (CT0106 P01 e).

The networks against the creation of a law enlisted their arguments: the regulation of clinical research is too dynamic to be regulated by a law (CT0106 P01 g); existing gaps in regulation will not be resolved in a law (CT0106 P01 g1); if law is thorough, it will stifle research (CT0106 P01 h); we already have in CONEP resolutions (CT0106 P01 h1) what FIOCRUZ proposes in PLS 200/2015.

Two actants emerge within the discussion of whether a law is really necessary. The first one regards international standards for the regulation of clinical research:

> “The international regulatory instruments for clinical research with human beings were edited precisely to give greater protection to research subjects, who are the most vulnerable side of the relationship. The Nuremberg Code and the Declaration of Helsinki, for example, presuppose the understanding that the advancement of science is not an absolute value and must respect ethical values and human rights. All this to prevent abuse against the dignity and integrity of people, as it happened in dark moments of human history, such as the experiments the Nazi carried out with Jews and other groups (Senator Otto Alencar, CT 0106 P01 j, in 29 /06/2016).

These norms would lend credibility to the resolutions created by CONEP, once the whole set of infra-legal norms was supposedly issued inspired by international regulation.

> “(...) it is important to highlight that the current system that regulates clinical research with human beings is primarily based on international standards, such as: the Nuremberg Code; the Declaration of Human Rights; the Declaration of Helsinki; the United Nations – UN International Agreement on Civil and Political Rights; the International Ethical Guidelines for Biomedical Research Involving Human Beings of the World Health Organization – WHO; and the International Guidelines for the Ethical Review of Epidemiological Studies, among others (Deputy Hiran Gonçalves, CT0106 P01 m, on 10/29/2018).

The second actant is an opinion written by the the lawyer Luiz Roberto Barroso, now Minister of the Federal Supreme Court.

> In this regard, we reproduce the understanding expressed by jurist Luiz Roberto Barroso, current Minister of the Federal Supreme Court, whose clear speech follows:
>
> *The exercise of the regulatory power – at least in the terms in which it is traditionally understood – presupposes a previous formal law that disciplines the matter to be regulated.*
>
> *In this case there is no formal law in Brazil that disciplines the ethical evaluation of clinical research with human beings: the only existing normative acts on the matter are resolutions of the National Health Council. In this context, the validity of these resolutions cannot be assessed from of material parameters contained in the law itself – since they do not exist.*
>
> .....
>
> *[...] in view of the normative system currently in force in the country, CNS resolutions are not competent to create and impose a system of ethical control of clinical research. Such finding, of course, does not disqualify the Board, its importance and*

> *the legitimate motivations that inspire its performance. However, its legislative nature nature are not aligned with the institutional arrangement in force in the country and with the democratic principle itself. (Senator Otto Alencar, CT 0106 P01 k, on 06/29/2016)*

If the first actant (international norms) had the effect of rescuing the dignity of the set of infra-legal norms that developed over the last few decades, the second actant (in Minister Barroso's opinion), held his position that a law is necessary, since only a law produced by parliamentarians or representatives of the people (and not by technicians) would ensure the democratic principle in the regulatory choices that should govern clinical research activity, besides providing the propagated "legal security".

Minister Barroso's opinion covered the entire legislative process, almost to the point of 'framing' (a technique described by Latour (1999) that promotes the exposure of the argument to as many people as possible in order to reduce the intensity of the controversy), but a mobilization, in the *Callonian* style (CALLON, 1986), was proposed by the rapporteur of the Science and Technology Committee (CCT), 'Afonso Mota+deputy', already in the course of PL 7082/2017:

> "However, before considering the explanation of the changes proposed by this rapporteur, I emphasize the importance of regulating the issue through a law approved by this Parliament. With the approval of this project, I believe that greater legal certainty will be ensured for those involved in clinical research on human beings. In addition to establishing a series of rights and obligations for those involved, the PL authored by senator Ana Amélia also has the merit of defining the national system of ethics in clinical research with human beings, clearly distributing the attributions of the different instances, thus avoiding overlapping of functions and in a last analysis, making the process of ethical analysis more rational.
>
> While I recognize the importance of establishing rules through law, I also understand that law has its limits. It is impossible for the legislator to glimpse all the issues that permeate the subject not to mention glimpsing all its vicissitudes. This statement is even truer compared to complex and dynamic topics such as the one under analysis. Therefore, I understand that it is up to the legislator to establish general rules, detailing only aspects considered essential. The Executive Power, through its bodies, will be responsible for detailing via administrative acts what is lawfully established by the Parliament. Therefore, many demands sent to this rapporteur were not included in the bill. (Deputy Afonso Mota, CT 0106 P01 l, on 12/14/2017).

Deputy Hiran Gonçalves of the Social Security and Family Committee (CAS) endorsed:

> "When creating the new system it is necessary to establish minimum criteria and premises for its composition and functioning. Therefore, Law must establish the minimum conditions and the regulation must deal with its functioning. (Deputy Hiran Gonçalves, CT 0106 P01 n, on 10/29/2018).

The need for a law to affirm democracy and provide legal security to the rules that safeguard rights and obligations of the parties involved was recognized. However, limits to the law were recognized, which cannot foresee all the issues that arise in the clinical research process.

For this reason, a law must establish general rules, and the Executive Power will issue administrative acts to detail the rules in technical and specific matters through its regulatory agencies.

The third type of translation described by Latour (1999) is close, and the opinion of deputies Afonso Mota – approved in full – followed by the endorsement of deputy Hiran Gonçalves, also approved by his peers, seems to have closed the first black box of this process.

However, a historical review of everything that was developed by CEP/CONEP reopens the black box and resumes the discussion on the relevance of a law for clinical research issued by the National Congress.

'Dirceu Greco+doctor+Brazilian Society of Bioethics' rescues the development process of the regulation that resulted in Resolution CNS 466/2021 and predicts that the law that will result from PL 7082/2017 will put an end to all this issue:

> "From 1966, when the resolution for the Declaration of Helsinki in 1964 first appeared, until this became a position. It started there by request. The Nuremberg Code quoted here is from 1947. Then, in 1964, as I said, there was the Declaration of Helsinki, which became the 2013 version. UNESCO has a spectacular declaration that all countries signed, which is the Universal Declaration of Bioethics and Human Rights, and the one I showed you in 2016, which is also about this. So there is a story of attempted change. The proposal that is being made [PL 7082/207] here today is to end this matter. There is intense pressure on national declarations, but they first came internationally.
>
> (...)
>
> "What are the current characteristics of Resolution 466? One of them is independence. (...) Amplitude is another point I consider important to discuss when we get to deeper discussion. Other features are: social control: turning a dynamic process into a law is complicated. There is a framework, there is a risk. And how do you change that later? Think about it: this took all this time, since 2015 to come out, it was supposed to come out in 4 years. Did the process change? So, the law has to be changed. (Dirceu Bartolomeu Greco, UFMG, CT 01.06 P01 o, 12/06/2018).

Minister Barroso gives his opinion again in order to hold the critics' rejection towards PL 7082/2017:

> "(...) the members of the Clinical Research Alliance Brazil, which, for those unaware, brings together research entities, researchers, medical societies, such as the Brazilian Medical Association, the Brazilian Society of Clinical Oncology, the Brazilian Society of Endocrinology and Metabolism, in short, professionals who like me have been working in this area for over 20 years.
>
> ....
>
> We consulted a legal authority, the eminent jurist Luiz Roberto Barroso, now Minister of the Federal Supreme Court, who gave the following opinion: *A system without law: Clinical Research and Ethics in Research in Brazil. The Brazilian System of ethical review in research suffers from a serious problem regarding its legal validity due to the absence of a law that distributes competences and disciplines behavior.*
>
> 2. The bodies of the CEP/CONEP system when performing their administrative and normative functions are subject to the constitutional principles that rule public administration. (Jaderson Sócrates Lima, CT0106 P01 p, on 12/06/2018)

However, for the first time, Minister Barroso's opinion is challenged by new relations that change the direction of the actant´s behavior.

The opinion, even supported by the acting “minister”, was actually produced by a lawyer, the same Luiz Barroso mentioned above. Later, after becoming a minister, he would have judged several processes in which the right to medicines was recognized, although not registered in the country, which shows the possibility of attributing rights even if there is no law on the subject.

> “Notice that one thing is Dr. Barroso's opinion at the time he was a lawyer and at the time a bill was not being discussed. If you have an opinion that says that some resolutions create a certain legal fragility, this seems to make sense in a way, although we have many court decisions based on resolutions – and there are many – and opinions including that of the Attorney of the Republic and everything else. Everything is fine with that.
>
> Later, as a Minister, when the right to judicialization of patients was being discussed in the Supreme Court, Minister Barroso stated that medicines not registered in the country were not prohibited from being prescribed by court decision – and of course with medical support and subject to a series of conditions placed on his opinion. (Jorge Venâncio, CT0106 P01 h, on 12/06/2018)

This is as saying that the opinion that endorses the position of those in favor of PL 7082/2017 is the product of the "lawyer+Barroso" network actor, while the "judge+Barroso" would be more inclined to make relative the legal certainty thesis, benefiting those who consider the current regime to be the more appropriate.

‘The need for a law’ thesis as a requirement for predictability in the regulatory process and demonstration of the democratic legitimacy of the attribution of rights and obligations to those involved in clinical research was rejected by the ‘incompleteness of the law’ to rule complex and dynamic situations, which would only be feasible if such attribution was exercised by experts, based on good practices developed by international standards and which inspired the construction of the current regulation of the CEP/CONEP system.

So, the performativity of international norms on current infra-legal acts would be enough to balance the Brazilian regulation that seeks to reconcile safety and agility in clinical research.

However, new actants are recognized in the relations of power that arise from the associations that constitute the CONEP. This Council would have been taken over by political interests that abuse regulatory power, although these same interests would have been justified precisely to confer popular participation in its constitution.

A new controversy arises regarding whether the regulatory legal framework (to be produced by PL 7082/2017) (a) reinforces the democratic principle of establishing an artifact made by those who represent the popular will or (b) suppresses social control by setting stricter rules on who will integrate the CONEP.

It is the controversy over the type of democracy, participatory or representative, that one wants to establish in the regulation of clinical research.

These are, after all, the interests behind the issue regarding whether or not a law is necessary.

More than that, controversy evolves to become a political debate about who or what will make the compatibility between interests in the development of pharmaceutical technology and the safeguarding of research participants.

Regulation abandons the spectrum of relations that regard it as the "good guy" or the "bad guy" and becomes an agencement supported by network actors who seek to resolve the recalcitrance of their ambivalence to reconcile interests through devices that control the development process of drugs against adverse effects of their use.

Controversies come to discuss not only (a) what dosage of regulation one wants to exert on clinical research, but above all (b) who will make this decision.

The ethical instance of regulation, headed by the CEP/CONEP system, is reassembled. This is the topic of the following narrative.

8.2 Narrative 02: the CEP-CONEP “system”[22]

Controversies surrounding the regulation of clinical research and the performative effects that follow it shift to particularize the clash around the artifacts of its ethical aspect, which has been until now explained by the relations that materialize what we call CEP-CONEP "system”, and which has been the main target of the interventions recommended by PLS 200/2015 (PL 7082/2017).

The opening of this black box replicates the entire discussion about the regulation of clinical research and its emblems characterized by the clash between efficiency versus safety, autonomy of individual will versus protection of life, rights of participants in a clinical research versus those of patients waiting for treatment.

But here the debate creates gaps in the reification of administrative bodies that present themselves as a ‘control system of ethical regulation’ and that strictly speaking configures another packaging of heterogeneous relations that despite promote instability advocating control.

[22] Link of the map of controversies of the topic “CEP-CONEP system”: https://bityli.com/74QxrC

The search for security, predictability and stability has been intensified precisely because CONEP and CEP's are accused of not promoting such results.

The law that may arise from PLS 200/2015, and which aims to disaggregate CEP-CONEP actants, intends to create a dimness of explanation in the decision-making processes that emerge from their actions.

Little by little the destabilizing regulation gives room to an allegedly stabilizing law. And this law works for the destabilization of the institutional actor that struggles to maintain the configuration status quo.

It is really interesting to glimpse a movement of stability versus instability that slides between subject and object (or is it the other way around?), from infra-legal regulation to law (search for stabilization), from the current macro-actor to its reconfiguration (search for destabilization).

The challenge is to follow the work of the actants to understand the performative mentality of these movements. The attack to the CEP-CONEP system is due to the accusation of its inefficiency and discredit. Counterattacks invoke the system's international credibility, history and evolution. In the end, the controversy over the model of social control exercised by CONEP gained notoriety. It is the struggle over who or what will ultimately control regulation.

a) The CEP/CONEP system is (or not) efficient (CT03.01)[23]

Ethical security in Brazilian clinical research is kept “under lock and key”. This is the conclusion of the network “Aliança Brasil Pesquisa Clínica+Fabio André Franke” in one of the sessions of the Federal Senate:

> “First, the approval of the CEP from abroad and then of a local coordinating CEP; then it is centrally approved by Conep; after that it goes back to the local CEP appraisal; later, we need to wait for Anvisa's approval; and finally, we have to wait for the product to be imported. This time exceeds one year in average. What happens in practice? There are 700 CEPs throughout Brazil. A second centralized approval is necessary. With each new questioning, the period of 30 to 60 days is renewed, which, depending on the pending issues and resources, is even longer, accumulating issues to be solved and the process to get stuck. (ALIANÇA, Fábio Franke, CT0301 P01 g, on 11/10/2015)

Criticism is on the excesses of control by a decentralized system and based on a “double instance” of evaluation of research protocols, making it bureaucratic and time-consuming. This criticism is reinforced when comparing ethical control with the practices of other countries:

[23]Link of map of controversies CT03.01: https://bityli.com/74QxrC

> The Brazilian regulatory system is quite interesting. Some countries opt for a sequential assessment system; others for a parallel one. We are very creative: we have a parallel sequential system. So, the project enters the local Ethics Committee; later, it is sent to Anvisa and Conep. (ICESP, Paulo Marcelo Hoff, CT0301 P01 d, on 11/10/2015)

In Brazil, this dual assessment system, which is at the same time sequential and parallel, results in an overlapping of ethical control involving both national (CONEP) and local levels (CEP).

And here network defenders of PLS 200/2015, shrewdly hastened to weaken their enemies (LATOUR, 1999) putting them to fight with each other: this duplicity and overlap would end up by disqualifying, weakening or emptying the CEP's works to the detriment of CONEP.

> "For 20 years double assessment has been based on the disqualification of the opinion of the institution's CEP. Thus, very often the opinion of the local CEP is of no use at all. And we are wasting the time of people who are dedicated to this so that there is central control. This generates all the slowness and bureaucracy. So, the double approval takes away this autonomy. (ALIANÇA – Fabio Andre Franke, CT0301 P01 g1, on 11/10/2015).

The reaction comes through numbers: there would be no relevant overlap, since "only 1.6% of the protocols go to CONEP and the other 98.4% are processed exclusively in local CEPs" (CT0301 P01 g2), states the 'CONEP +Jorge Venancio' network.

However, as it is necessary to qualify the enlisted data to "stack" the rhetoric quickly, the categorization of projects ("projects for new drugs", "international collaboration projects" and "projects involving biological material") are called to reject superficial and descriptive statistics, thus raising criticism to the system:

> "Dr. Jorge may be correct, in the sense that most projects do not go through Conep, but these are not the relevant ones. Projects with new drugs, those with international collaboration and projects that have biological material, all go through Conep. Unfortunately, what does not pass through Conep are those studies of lesser scientific relevance. They are important, but not cutting-edge studies. (ICESP – Paulo Marcelo Hoff, CT0301 P01 g3, on 11/10/2015).

b) The ethical control exercised by the CEP/CONEP system was (or not) distorted (CT03.05)[24]

Criticism to the inefficiency produced by a process of dual control instance, which is at the same time simultaneous, sequential and overlapping, shifts to criticism of the merits of the

[24]Link of map of controversies CT03.05: https://bityli.com/74QxrC

decisions produced by CEP-CONEP, to the point of asserting the deviation of purpose or misrepresentation of its attributions:

> “The CEP/CONEP requirements are not ethical. This looks like a doctoral thesis review: they ask to change "include" for "purposes of this study" and "following" for "described", that is, small things that have absolutely no impact, neither on ethics nor on the science that is being developed, but each of these demands brings the process back to the beginning; it has to be redone, sent back to Brasília, re-discussed. (ICESP, Paulo Marcelo Hoff, CT0301 P01 i, on 11/10/2015)

Absurdly, CONEP network also invokes the unreasonableness of research proponents coming therefore from the other side of the counter:

> “One of these days we saw a study that proposed to evaluate the depressive effect of a drug that is already being used, and it was proposed that a 'Suicide Dial' was created: "If you feel like committing suicide, dial 1; if you got depressed, dial 2" – and stuff like that. We were asked for a public hearing to explain why we did not accept this project, and when we explained our reason, the laboratory representative was astonished” (CONEP, Jorge Venâncio, CT0305 P01 b, on 11/10/2015).

There were countless examples to state the need and relevance of the system, leaving no doubt about its role as guardian of the safety of clinical research participants:

> “CONEP forbade dangerous and unnecessary procedures. The researcher proposes to perform a lung biopsy without any clinical indication; there is no benefit for the participant of the research; if he or she was being treated normally, that biopsy wouldn't be necessary. However, the researcher proposes to perform a lung biopsy, which can have consequences, even causing a pneumothorax and other problems. CONEP questioned this procedure (CONEP, Jorge Venâncio, CT0305 P01 a, on 11/10/2015).

However, 'Aliança+Fabio' network enlisted the oncology specialty to refuse authorization to the “CONEP+Venâncio+orthopedist” network, when it explains that:

> “The big issue is that this knowledge of tumor resistance is essential to plan new treatments. And what is it going to bring us? Evidence (and that is why it is performed only in the research environment) of some alterations in the tumor, some mutations in the tumor, which will then enable us to think about a new therapeutic possibility. Without this knowledge we cannot establish the best treatment for the patient. Take the case of breast cancer. We know that, between the initial tumor diagnosed in the breast and the metastasis there are 50 different types of mutations. So, the initial treatment is not the same given to metastasis. The biopsy has to be done, of course, and it has to be done in the research setting. If we don't do it in the research environment, we won't do it in the assistance moment. Why? Because we haven't tested it. So we have to test this hypothesis. This is now almost part of the research guideline for lung cancer, precisely because the number of mutations appears every day. (CONEP, Jorge Venâncio, CT03.05 P01 g, on 11/10/2015).

The rhetorical evolution that starts in the distortion of the system and is controversial regarding different views of technical specialties makes it clear that even with flaws CEP/CONEP is trying to do its best:

> We' don’t want to prohibit things unnecessarily. This is absolutely not the aim of Conep. We are doing our best to make the most of everything that is proposed, to do something that is beneficial to the research participant. That's the mind we're working

> with. So, it must be clear that we are not looking for problems. (CONEP, Jorge Venâncio, CT0305 P01 d, on 11/10/2015)

Once again CEP/CONEP is internationally recognized, and the comment is that it is "one of the most advanced systems in the world" (FIOCRUZ, Rodrigo Stabeli, CT0302 P01 a, 11/10/2015) and placed Brazil alongside the main countries that lead the world ranking in the development of clinical research regarding regulatory terms (Senator Aluísio Nunes, CT0302 P01 a1, on 12/16/2015).

The black box is closed to affirm the need and recognition of the system, but the controversy regarding what still needs to be improved and can be improved remains open.

> The lack of structure of the National Health Council to assume the functions of regulation and ethical inspection of clinical research in the country, in addition to the serious problems identified in the current configuration of the system, which make it slow and bureaucratic, have suggested the need of structural changes. (Senator Otto Alencar, CT0301 P01 k, on 12-14-2016).

c) A new law needs (or does not need) to discontinue the current CEP/CONEP system (CT03.03 P02)[25]

The CEP/CONEP system, which does not get rid of the flaw of being inefficient but shows its value, is then successful in preventing its demolition and accept small changes to the solid foundations of a construction built over so many years. History comes in.

If a law is going to be created, then let this new law not neglect the more than 20 years of experience gained during the development of the CEP/CONEP system:

> "Let's enjoy what you have. Not suitable? Of course it is not adequate, but we cannot simply tear 20 years of experience from the CEP/CONEP System, under penalty of starting from scratch and making all the mistakes we have already made so far. Let's enjoy with technique, efficiently, with the participation of all sectors this moment in which we are discussing; and let's discuss in a calm way (UFBA – Claudio Roberto Camperlingo Araujo, CT0303 P02 a, on 11/10-15).

The invocation of history to rescue the legacy of the development of standards by CONEP is due to the mobilization of several actants participating in this construction.

The network 'Dirceu Bartolomeu Greco+doctor' vocalizes the speech of the Brazilian Society of Bioethics in a legislative session of the Chamber on 12/06/2018. Involved with CONEP from the beginning, the actants report their base inspired by the "International Ethical Guidelines for Health-Related Research involving Human Subjects", prepared by the CIOMS – Council of International Organizations of Medical Sciences. Likewise, the Nuremberg Code,

[25]Link of map of controversies CT03.03 P02: https://bityli.com/74QxrC

from 1947, and the Declaration of Helsinki, from 1964, are rescued as having been “the basis of CONEP when the documents on which it was based appear”:

> “What is the Brazilian standard like? It is clearly based not only on protecting the vulnerable but also on justice and equity. It is about many things. Many of you who are listening now were not even born in 1988. The first National Health Council resolution regarded ethics in research; it was something impressive. (...) The proposal we are making here today is to put an end to this story. (...) As for the antecedents, there is intense pressure on the national declarations, but they came internationally first (CT 03.02 P01 c, on 12/06/2018).

Despite criticisms about the intention of PLS 200/2015 (PL 7082/2017) to "put an end to this story" [from CONEP], the contenders use the translational technique of "we are together" to assert: "no one wants to dismantle the system ”. The “ICESP+Marcelo Hoff” network points out:

> “Nobody wants to dismantle the system, we want to improve it so that it works for patients and for Conep, for researchers and society (CT0303 P02 b, on 11/10/2015).

However, CONEP insists on mistrust and warns that those interested in reforming the system could have called it to "talk" before this clash was taken to the Legislative Power. In this direction, criticisms are launched against the leading of the process: (a) the discussions could have been more advanced; and (b) the work of CONEP could have helped in these discussions:

> “I think this discussion could have started from a much more advanced level. We have a set of details on current system resolutions that could have helped the discussion go further, not start from the beginning. (CONEP, Jorge Venâncio, CT0303 P02 c, on 11/10/2015)

It is at this point, within the intra-relational clashes of the actants at play around the artifact “CEP-CONEP regulation”, that performativity is best expressed: the system is evolving, lawless (or because of the risk of emergence of a new law?).

d) The CEP/CONEP system is evolving (CT03.03 P01)[26]

From a performative point of view, the perspective of a law anticipates the effects it desires. There are numerous changes promoted by CONEP in an effort which seems to be to decrease the objectives of PLS 200/2015 (PL 7082/2017):

> We are in the final phase of elaborating some complementary resolutions to the master resolution, which is currently Resolution nº 466, of the National Health Council. We are making a risk classification and a differentiated procedure according to the degree of risk of each protocol. (CONEP – Jorge Alves de Almeida Venâncio, CT0303 P01 a, on 11/10/2015)

[26]Link of map of controversies CT03.03 P01: https://bityli.com/74QxrC

CONEP referred to resolution number 506 issued on 02/03/2016 that established a new differentiated accreditation process for Ethics Committees according to the degree of risk in each protocol, which practically eliminated the need of a "double analysis" that was so criticized in the processing of the bill.

In case of "minimal risk" the protocols are only registered with no need of ethical evaluation. "Low risk" protocols are analyzed by a CEP rapporteur who only sends them upon request; the processing should take about ten days. "Moderate risk" protocols are subject to the same procedure in force, and are analyzed by the rapporteur and by the board of a CEP. Finally, high-risk protocols have a single procedure in Ethics Committees accredited for this function. In this case, CONEP will operate only as a stage of appeal, regulating, supervising and harmonization of the system.

The efforts of CONEP continue: "*We are decentralizing, but without losing the harmony of the set of decisions. CONEP is considering to replace the current model by a new system"* (Jorge Venâncio, CT0303 P01 b, on 11/10/2015). It is demonstrated that besides decentralizing the system, Resolution 506/2016 would reduce analysis periods, thus increasing the efficiency of the process.

> In the current model [Resolution 466/2012], the protocol goes first through the local CEP and then to CONEP when the risk is high, and then to the participating CEPs. In the new model [Resolution 506/2016], the protocol goes directly to the accredited CEP, and then the local CEPs would only check local issues that generally have a fairly quick processing. Thus, the analysis period can be reduced to something around 30 days within the accredited CEP. (Jorge Venâncio, CT0303 P01 b, on 11/10/2015)

This effort was noticed as an (opportunist?) reaction to PL 200/2015. The network "Ana Amélia+Senator" noticed that "the institutions began to move":

> "It is a coincidence that, at the moment that PL 200 started to be processed in the Senate, the approval time of Conep sped up. They did it as expected (ICESP – Paulo Marcelo Hoff, CT0303 P01 c, on 11/10/2015).
>
> "When we discussed this for the first time there was a movement, as recognized by Dr. Paulo Hoff. Institutions began to move. And for the first time, I see that Conep is open to accept that the project can be improved. I said that it doesn't start perfect, otherwise it wouldn't have to go through the commissions. From here it goes to another commission. But, for the first time I see a willingness to accept (Senator Ana Amélia, CT 0206 P01 b, on 11/10/2015).

However, according to CONEP, evolution has taken place long before the advent of PL 200 and despite the legislative work:

> (...) it has nothing to do with the current discussion about PL or anything like that. We are getting better results now, as a result of the work we have been doing for two and a half years. However, it has absolutely nothing to do with a momentary thing or something of the kind (CONEP – Jorge Venâncio, CT0303 P01 d3, on 11/10/2015).

Whether or not the performative effect of the actant PLS 200/2015 (PL 7082/2017) on the regulation of clinical research is recognized, the fact is that several changes happened after the consolidation of guidelines and regulatory research standards, which resulted from Resolution CNS number 466/2012.

After 4 years without the creation of any standard to update the system, in 2016, Resolution No. 506/2016 was published (already reported), and changed the way CEP's are accredited. From that year onwards, just as the work of PLS 200/2015 began to intensify, numerous other resolutions began to emerge. We highlight the following: Resolution No. 510/2016, which started to discipline clinical research in the human and social sciences; Resolution No. 563/2017, which regulated the participant's right in research with ultra-rare diseases; Resolution No. 580/2018, which disciplined strategic research for SUS; Resolution No. 647/2020, which regulated the process of designation and performance of CEP members appointed by social control entities; and Resolution No. 656/2021, which provided for extension of mandate within the scope of CONEP.

e) The CEP/CONEP system and social control (CT03.04)[27]

Democracy is an underlying actant because of the way it was associated with the networks that were formed during the works of deconstruction and reconstruction of clinical research, its regulation and the CEP-CONEP macro-actors that were revived throughout the process.

Stylized at first, in the 'opinion+lawyer+Luiz_Barroso', 'democracy' was an ally in the search for the reconstruction of the system under the aegis of law, since regulation being supported by infra-legal norms, democracy would be underrepresented by non-mandatory agents of the popular will.

However, it is also enlisted by defenders of the current infra-legal model, who accuse PL 200/2015 (PL 7082/2017) of weakening the 'social control' erected under the nomination criteria of CONEP members.

Social control enters into relations as the third guiding element of the regulatory model advocated by the actants. It is not just 'efficiency' and 'ethics' that are in dispute, but the power emanating from the so-called 'social control' that is instrumentalized by the right to participate in the production of resolutions issued by CONEP (or to limit its prerogative).

[27]Link of map of controversies CT03.04: https://bityli.com/74QxrC

> “Social control and ethics in research cannot stuck the evaluation of research protocols. (FIOCRUZ, Rodrigo Stabeli, CT0304 P01 b, on 11/10/2015).

The current system establishes the obligation of 'social control' through the participation of representatives of research users in CEP's:

> “The participation of users in Ethics Committees is a very positive experience nowadays. There is a requirement for one user in each Ethics Committee; and, spontaneously, large committees, such as the HC Committee, the USP Committee, the Syrian Lebanese Committee, place two or three users representatives in their own committees (CONEP, Jorge Venâncio, CT0304 P01 a, on 10/11/2015)

Also at CONEP, social control is established not only through the representation of civil society in general, but also by members who have “technical profiles" and are "highly qualified":

> “Now, I want to give you a little more practical idea. To give you an idea, today we have at Conep, for example, the former Dean of the Federal University of Santa Catarina, the Dean of Postgraduate Studies at the Federal University of Acre, the Dean of the Health Sciences Center at PUC do Paraná and the Dean of UNORP from São José do Rio Preto. Therefore, we have a great technical qualification within Conep, but at the same time – based on information of the Council, or sometimes even information of CEPs – we have representatives for celiac, for Alzheimer's disease, for Gaucher disease, we have an indigenous chief, because we have to analyze projects with Indians – a Xavante chief is part of Conep and has a very active participation at several times –, and this does not affect the technical qualification that is given by the other members (CONEP, Jorge Venâncio, CT0304 P01 a1, on 11/10/20215).

The choice of members of these bodies follows criteria considered "objective" by CEP's and by CONEP:

> “At CONEP there is a whole set of regulations. There are two resolutions on choice criteria to define what users are and how they are chosen. It is a positive experience that must be maintained.
>
> "The CEPs are nominated by the directions, within the periods in which there is replacement. It is not possible to make changes between terms of office. Otherwise, the CEP has autonomy from one election to another. When the electoral period comes, some institutions even hold elections among their members; others have the board nominating and nominations among those from the previous committee. The term of the ethics committees are of three years. (CONEP, Jorge Venâncio, CT0301 P01 j, on 11/10/2015)

It is worth to remember that according to Resolution number 446/2012, CONEP is composed by thirty members, twenty-two of which appointed from the CEP's and eight appointed by the CNS. The criteria for this selection process are explained by the 'CONEP+Jorge_Venâncio' network:

> “Each committee nominates two names at election time; the election is half/half, every two years; the term is of four years, but in the election, half of the members are renewed every two years. The committees appoint two members, who may be from the committee or may be someone else they consider to have the necessary requirements to participate in Conep – each committee has autonomy to make nominations –, besides, a mixed commission is organized, which is half Conep, half Ministry of Health; then this commission analyzes these curricula and makes a

> proposal to the National Health Council. So, this is the mechanism to compose Conep with these 22 members appointed by the ethics committees.
>
> "As for the 8 members who are directly appointed by the National Health Council – which are the remainder to complete the 30 members – the only restriction is that they are proportional to each of the groups. So there are 4 user members, 2 members from the health workers group and 2 members of the Government. This is the only existing restriction, and then the National Health Council is free to nominate the members it deems convenient, within these 8 vacancies; however, most of them have well-developed technical capacity and come from base committees. (CONEP, Jorge Venâncio, CT0304 P01 c1, on 11/10/2015).

At least within the CEP's, social control has improved, as verified by the issue of Resolution number 647/2020, which regulated the process of designation and performance of CEP members appointed by social control entities called RPP (Research Participant Representatives), establishing rules on the profile, performance, rite of nominations and relations that the RPP must keep with the CEPs they participate.

Although it is noticed once again the performativity in the effort of the CEP-CONEP system in granting objectivity, impersonality and fractionation in the representation of several political power nuclei as members of these bodies, the fact is that the controversy surrounding "social control" involves deeper relationships.

The power one tries to build does not involve only the RPP, but science itself and the artifacts that confer legitimacy to the technical and scientific authority, as if socio-political actants were not also present in them.

> "We cannot mix up research and science with politics and ideology. Research is pure science and that's what we're dealing with, it's not ideology. As much respect as we have for all instances of popular consultation, we have to understand that research in the biomedical area is for specialists, researchers, and those who know and have studied for a long time to do research and find out if a new drug, whether or not a new drug will be suitable to treat a new disease or an existing one, such as cancer and Alzheimer's. So, we cannot mix up ideology with science or mathematics. It is an exact matter and researchers know it. This is what we are dealing with: the pain of thousands of families who, manifested themselves enormously when the controversial cancer pill was discussed here because everyone has an urgency for the patients' cure (Senator Ana Amélia, CT0304 P01 d, on 15/ 02/2017)

The CEP-CONEP system struggles to depoliticize the participatory democracy chosen to legitimize social control in the constitution of its members.

Opposing networks claim that depolitization is impossible and want to introduce, under the primacy of a law that remodels the system, representative democracy, which is more technical, more scientific and more reduced in the construction of communication channels between the State and society.

The recommended model denounces the politicization of the CEP-CONEP system as a driving force behind inefficiency, distortion and delay in the process of approving research protocols.

The current model denounces the intention of the PLS 200/2015 (PL 7082/2017) to make the process technical and far from the interests of the clinical research participants, and democratically insufficient.

It is as if they were turning the "Clinical Research Participant Statute" into a "Clinical Research Sponsor Statute":

> "The system is designed to protect the vulnerable side that is the research participant. The main flaw I think there is in the current opinion is this: it is concerned with defending the sponsor, not the research participant. (CONEP, Jorge Venâncio, CT0304 P01 e, on 12/06/2018).

In the clash and movement of networks one can see that "science" and "politics", as well as "participatory" and "representative" forms of democracy are all being enlisted for the definition of control over regulation.

It doesn't matter so much which institutional actors – CEP's, CONEP, with these or other designations – will constitute the regulatory "agencement". What matters is to know which relations involved will win the fight. This is the subject of narrative 03.

8.3 Narrative 03: The Bill

PLS 200/2015, converted into PL 7082/2017, has been in force since when the reassembly process of clinical research and the CEP-CONEP system the artifacts of the Federal Senate and the Chamber of Deputies came in. However, it is necessary to explain the Brazilian process of creating laws in its four phases.

In the first phase, which is the proposition phase, a federal deputy or senator presents a bill to the Chamber or the Senate so that its processing begins. As the Brazilian system is bicameral[28], the projects of ordinary laws are analyzed by both legislative houses. The order in which this occurs does not matter, which means that the Chamber of Deputies can analyze before the Federal Senate or the other way around. PLS 200 started in the Federal Senate, which was the 'initiating house', with the Chamber of Deputies acting as the 'reviewing house' (figure 18).

[28]Bicameralism is the regime in which the Legislative Power is exercised by two Chambers, the Lower Chamber and the Upper Chamber. In Brazil, they are represented by the Chamber of Deputies and the Federal Senate, respectively.

Figure 18 Legislative Process of PLS 200/2015 (PL 7082/2017)

Source: Chamber of Deputies

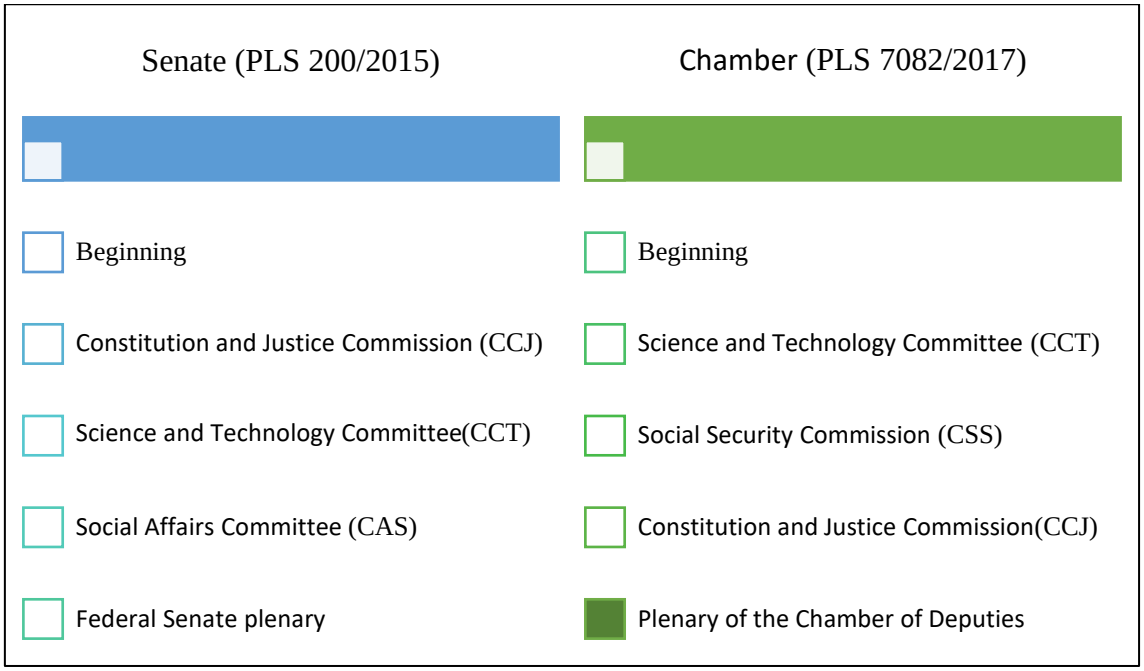
The second phase is the discussion. The project goes through different and successive thematic commissions, composed by collegiate members of parliamentarians. The committees debate the project, which can be approved, rejected or modified.

The third phase is the deliberation, where the project is analyzed by the plenary of the legislative house. If the project is approved by the initiating legislative house, it is then forwarded to the revising legislative house, where it will be analyzed again by the thematic commissions and by the respective plenary. If the reviewing house makes changes to the project, it is returned to the initiating house for further consideration.

Once these phases have been completed, the fourth phase is enactment, in which the project is submitted to the head of the executive branch for sanction (when it will then be converted into a law) or veto (in which case the project returns to the Legislative Branch for deliberation on the overthrow or maintenance of the presidential veto).

The intra-relational activities of the regulation of Brazilian clinical research, mapped during the development of the thesis were those that occurred in the work of the commissions of the Federal Senate (which acted as the initiating house of PLS 200/2015) and of the commissions of the Chamber of Deputies (which operated as a reviewing house for PL 7082/2017). Table 06 demonstrates the commissions that acted during the course of the project:

Table 6 Proposal path



Source: Federal Senate and Chamber of Deputies

In each commission, different actants participated in the networks that traced the inter and intra relations of the regulatory artifact that has been developed under the epithet of the "CEP-CONEP system".

In the reassembly, not only the meaning of the regulation was transformed, with performative effects on the regulated activities, but also translations of these reframed realities were implemented through the approval of legislative amendments (or proposed changes to the project that were made during discussion and deliberation) that gave rise to the different versions of the project.

When mapping the controversies of interests, I identified an itinerary of versions of the CEP-CONEP system, sometimes explained, sometimes disaggregated by the work of the networks that are still being reassembled with no prospects that the black box will be closed.

What is sought in this narrative is only to map the dynamics of the amendments to the Bill submitted to the above-mentioned Senate and Chamber committees.

The analysis of the translations involved will depend on the integration of the three narratives, which will be carried out in the next section.

It is also important to consider that the version of the project that is in the Chamber of Deputies and approved by the CCJC, until the conclusion of this thesis will still be submitted

to its Plenary (third phase) and then returned to the initiating House (Federal Senate), where many controversies can still be raised.

Among the various trajectories that can be narrated, I focused on those that deepen the organizational remodeling of the assemblage of the ethical instance of the regulation of clinical research, as already described in narratives 01 and 02, namely: a) controversies about the disputing actants control over the regulatory artifact; b) the controversies about the splitting of the committees of research ethics (CEP) into independent ethics committees (CEI); c) controversies over the proposed elimination of dual instance from the system; and d) controversies about the composition criteria of the organs of the system.

a) Who controls the ethical regulation system - CONEP under threat - CT 02.01 P01[29]

The proposal of PLS 200/2015 was to create an "ethical review body", whose mission would be to protect the integrity and dignity of research subjects and contribute to the development of research within ethical standards.

It is interesting to notice that during the processing of PLS 200 by the CCJ this "instance" does not include the CONEP, but says that the functions of the "ethical review body" will be exercised by CEP's and CEI's (Ethics Committees Independents), the latter to be created by the new law.

The CONEP actant, who before the PLS 200/2015 ignored the movement, feels and attempt of "interest" by the other actants (CALLON, 1986), but reacts by enlisting its representatives in the Senate for a counterattack.

The network "senator+Randolphe+Conep+internal regiment" presents Amendment number 13 to the Science and Technology Commission (CCT), proposing that the board of CEP's and CEI's operate as a "National Body for the Control of Ethical Review of clinical research" associated to the national direction of the Unified Health System (SUS), and that CONEP (National Commission for Research Ethics) be reestablished associated to the National Health Council (CNS).

CONEP's struggle continues throughout the work of all commissions and the rhetorical argument of loss of social control is recurrent:

> "If PLS-200/2015 is approved as it is, there will be no longer the participation of user representatives and popular participation, which is not desirable in a society in which

[29] Link of Map of Controversies CT02.01: https://bityli.com/74QxrC

> social control is widely recognized and valued (Senator Randolfe Rodrigues, CT 02.01 P01 g, on 02-13-2017).

However, a new actant also appears in the network: volunteering, which would be exempted with the extinction of CONEP, and therefore there would be an increase in the costs of maintaining the new system.

> Conep's permanence in the CNS is the best guarantee of its independence, which is so necessary for an effective protection of research participants. Furthermore, under the proposed conditions, it would not be possible to maintain the voluntary system that currently exists at Conep, which would significantly increase expenses related to the operation of the new system (Senator Randolfe Rodrigues, CT 02.01 P01 h, on 13-02-2017).

Amendment number 13 is rejected, since the other CCT actants, pressed by the influence of the delay, which had been efficiently tied to the CEP/CONEP system, insist on the deposition of CONEP, and propose association to the "National Body for Ethical Control of Clinical Research" to the National Health Surveillance Agency (ANVISA) instead, which would in addition to its health attributions have the technical, scientific and professional competence to also regulate and supervise the ethical control of clinical research in the country .

CCT changes the proposal from CCJC, and approves a replacement text through Amendment number 22 to PLS 200/2015, clarifying the proposal to create a "National System for Ethical Review of Clinical Research" that will include a national body for ethical control of clinical research associated to ANVISA, and a local body for ethical review formed by CEPs.

Therefore, the proposal that prevails in the CCT removes from CONEP any attribution regarding ethical regulation of clinical research.

As to the attribution of ethical control to ANVISA, CCT members recognize that there is a difference between the activity of health surveillance and ethical control, but believe that since both have the same objective (protect the population's health) it is possible that these two functions fall under responsibility of ANVISA.

The project is now going through the Social Affairs Committee (CAS), which formulates a new proposal (Amendment number 25, replacement): to make terminological changes from the expressions "ethical review body" to "ethical analysis body" and "National Board of Control of Ethical Review of Clinical Research" to "National Board of Research Ethics".

According to Amendment number 25, the "ethical analysis body" would be associated to the Ministry of Health, under the coordination of the Department of Science, Technology and Strategic Inputs, and no longer to ANVISA.

It was considered that if the national instance belonged to ANVISA, this agency would be responsible for almost 800 Research Ethics Committees in the country, besides being in

charge of implementing the accreditation process of these committees. As ANVISA has limited staff, it was understood that adding these responsibilities to the agency would aggravate the already existing burden. The consequence would be that the law would affect precisely who should not be burdened: the research participant in their safety.

The proposal was reformulated and the following was included in article 7 of Amendment number 25 of PLS 200/2015: “the national system of ethics in research with human beings is formed by: I – a national instance of ethics in clinical research associated to the Ministry of Health; and II – an instance of ethical analysis of clinical research represented by CEP's”.

What is behind this movement to disassociate from the ethical control of clinical research of CNS (and CONEP), and then of ANVISA, was the *Callonian* 'mobilization' tactic consisting of the formation of a coalition of the main actors and the silencing of the dissenting voices, so that the affirmation of the politicization of the CNS prevailed and the lack of structure of ANVISA to be in charge of regulation and ethical supervision of clinical research in the country, resulting in a slow and bureaucratic system, thus suggesting the need for structural changes.

However, this change of associating the national instance of ethics in clinical research to the Ministry of Health was not enough to definitely decree the extinguishment of CONEP, which reacted, showing how essential it is.

Once the work of the Senate committees (CCJ, CCT and CAS) has been completed, PLS 200/2015 goes to plenary, and there is another attempt for the survival of CONEP, in the Latourian style, when describing his third type of translation: "what if we deviate a little bit?”.

The proposal came through the network “Senador+Humberto Costa”:

> “We understand that the CEP/CONEP board has developed important work in recent years. Therefore, our suggestion that the national instance of clinical research ethics be part of the Ministry of Health (the largest instance responsible for health promotion in the country), but with the mandatory participation of the National Health Council (the largest instance of popular participation in the promotion of health in the country) (Senator Humberto Costa, CT 02.01 P01 i, on 02/15/2017).

Notice that 'Senador+Humberto Costa' Network, who at the Plenary Session of 02/15/2017 defended the regulatory status of CONEP with a slight deviation (keep the ethical instance under the care of the Ministry of Health, but with the participation of CNS in the formation of its collegiate), is not the same network "Senator+Humberto Costa" that on 06/29/2016 at CAS defended the total removal of the regulatory body from the responsibility of CONEP/CNS:

> The other point concerns who should be responsible for this national instance of ethical control of clinical research; here there is a proposal of its association with Anvisa. (...) I know that many people from CNS will not like my position, but I think it is not under the proper responsibility. I think that the Council, as a social control

> body, does not seem to be the ideal space for standardizing this ethical review that is carried out permanently or as an appeal instance when there is no agreement, but I also have doubts about whether the best is Anvisa, since Anvisa will be responsible to register those drugs, monitor their production and inspect quality, so I think Anvisa already has too much to handle and is not able to deal with all this; it may be another one that won't work properly. (CT 02.01 P01 j, on 06/29/2016).

The work of the initiating house ends despite the intensification of the controversy, as those actants who resisted the project did not accept the end of CONEP and the victory of the Ministry of Health over the CNS. The substitute bill contained in Amendment 25 is approved by the plenary of the Senate and PLS 200/2015 becomes PL 7082/2017, which is now being processed by the committees of the Chamber of Deputies.

PL 7082/2017 begins its processing by the CCTCI (Commission on Science and Technology, Communication and Informatics), which accepts the pressure of CONEP, this time successful, to confirm that the national instance of ethics in clinical research must be performed by " bodies" that already have this role, that is, CONEP.

The enlisted actant is the country's highest law: the "Constitution of the Republic", which organizes things:

> The bill does not create an executive branch because if it did, it would be unconstitutional due to a flaw in initiative. In order to avoid such failure and aware of the need for regulation regarding the subject, the text of the Senate defined instances of ethical analysis in clinical research, which is perfectly compatible with the Federal Constitution.
>
> In spite of not creating any bodies, it seems clear to this rapporteur that the functions of the two instances should be performed by "bodies" that already have an important role in the analysis process of clinical research. Thus, having as a premise the search for legal certainty and effectiveness, I understand that the national instance should be performed by the National Research Ethics Commission (CONEP), and that the research ethics committees (CEP) should be in charge of ethical analysis . (Senator Afonso Mota, CT02.01 P01 k, on 12/14/2017).

Amendment number 02 of 2018 is approved. It establishes that: "The national instance of ethics in clinical research referred to in item XXV [of article 2 of PL 7082] shall be performed by the National Commission of Ethics in Research (CONEP) of the Ministry of Health".

But here comes the "separate vote + Luiza Erundina_Deputada" network, denouncing a subtle difference between the proposal approved by the Senate plenary and the one presented by the CCTCI of the Chamber of Deputies:

> "Our disagreement with the report presented relates to the national instance of ethics in clinical research, which is a current role of the National Research Ethics Commission (Conep) of the National Health Council.
>
> The groups of patients and specialists in bioethics disagree with the subordination of the national instance of ethics in clinical research to the Ministry of Health, coordinated by the Department of Science, Technology and Strategic Inputs, as proposed in the bill approved by the Federal Senate, for two main reasons: the withdrawal of participation from society and institutional independence.

> The National Health Council, to which Conep is currently associated is the highest decision-making body of the Unified Health System (SUS), formed by representatives of users, health workers, government and health service providers. It is understood that by disassociating this body from the National Health Council the proposal excludes citizens' from participating in the control of the research. Also, it threatens institutional independence by associating to operate with an executive government body; that's why we present Amendments 1 and 3 in this separate vote. (CCTCI, Separate vote, Deputy Luiza Erundina, CT 02.01 P01 l, on 04/18/2018)

If, on the one hand, the ethical body will belong to CONEP, as originally regulated by the current infra-legal regime, on the other hand, according to the new proposal, this body would no longer be linked to the CNS and would become subordinated to the Ministry of Health, under the coordination of the Department of Science, Technology and Strategic Inputs.

It's the maintenance of the wrapper, but with new content. It is the implosion of the CONEP network, keeping the same name to a new regulatory artifact.

The insurgency of the "discordant vote+Deputy+Luiza_Erundina" network did not prevail in the CSSF, and CONEP remained as an ethical instance of clinical research, but subordinated to the Ministry of Health.

However, CSSF tried to further deepen CONEP's reassembly by proposing new criteria for the composition of its members.

The "CONEP" artifact survived the clash, but is no longer associated to CNS, which will still be part of the new collegiate body. This is, at least, the proposal to be taken to the plenary of the Chamber, and later returned to the Federal Senate.

b) Who controls the ethical regulation system? Research Ethics Committees (CEP's) and the creation of Independent Ethics Committees (CEI's) (P0201 P03)[30]

In the efforts to rebuild the CEP-CONEP system, the research ethics committees (CEP's) were also attacked, but in other ways. PLS 200/2015 predicted that the "ethical review body" would be exercised by CEP's and by CEI's (Independent Ethics Committees).

According to the original text of the PLS 200, the CEI is defined as a:

> "independent organization constituted by an interdisciplinary collegiate, which includes medicine professionals, scientists and non-medical and non-scientific members, responsible for ensuring the protection of the rights, safety and well-being of the subjects of clinical research upon the ethical review of the research protocols" (Article 2, item VII).

CEP, in turn, is defined as:

[30]Link of the Map of Controversies CT02.01 P03: https://bityli.com/74QxrC

> "collegiate associated to a public or private institution that carries out clinical research of interdisciplinary nature, which includes medical professionals, scientists and non-medical and non-scientific members, responsible for ensuring the protection of the rights, safety and well-being of clinic research subjects through an ethical review of research protocols" (item VIII of article 2 of PLS 200/2015).

What was noticed was the creation of two different bodies, the first of an independent organization and the second associated to institutions that carry out the research, both constituted by the same composition criteria and similar competences.

The proposal was not understood by the networks of actants, being stated that:

> "the difference between the CEP (Research Ethics Committee) and the CEI (Interdisciplinary Ethics Committee) was not very clear, and the existence of both is questionable" (SBPC – Fernanda Sobral, CT0201 P03 a, on 11/10/2015).

CONEP joined ICESP to express that they "did not see a need of the CEI's" (CT0201 P01 b1 and b2, on 11/10/2015).

The "FIOCRUZ+Rodrigo Stabeli" network joined the "CONEP+Jorge Venâncio" network to denounce the risk that the CEIs represent a subordination of ethics committees to interests other than those that exclusively guarantee ethics and preservation of human beings (CT0201 P03 b, on 11/10/2015):

> "The current CEPs have expenses that are financed by their own institutions (hospitals, universities, health departments etc.). The fear is that there will be CEIs from the very companies to analyze their own research protocols, which seems to us to be an evident, flagrant conflict of interest (CONEP – Jorge Venâncio, CT0201 P03 c, on 11/10/2015) .
>
> "The creation of Independent Ethics Committees is not necessary, as this would actually characterize a possible subordination of ethics committees to different interests and not to guarantee ethics and preservation of human beings, exclusively (FIOCRUZ – Rodrigo Guerino Stabeli , CT0201 P03 c2, on 11/10/2015).

With no resistance from the network that supports PLS 200/2015, the idea of creating the CEI'S was abandoned in the CCT of the Federal Senate, with the approval of Amendment 12:

> AMENDMENT No. 12- CCT (to PLS No. 200, of 2015) – "Delete item VII of art. 2 of Senate Bill No. 200 of 2015, and where in the text of the bill the expressions 'or by the independent ethics committee (IEC)' and 'or IEC' appear". (Federal Senate, CCT - 03/15/2016)

c) Dual or unified instance of research ethics - CT02.02[31]

Despite the performative effect generated by PLS 200/2015 that resulted in the creation of CNS Resolution number 506/2016, which practically puts an end to the problem of overlapping attributions of CONEP and CEP's, thus eliminating criticism about the "double

[31] Link of the Map of Controversies CT02.02: https://bityli.com/74QxrC

instance" of the system, the theme advanced in the legislative works of the networks that feed the clash of " new regulation" of clinical research.

On the one hand, the network led by CONEP defends the sufficiency of what has already been implemented by CNS. On the other hand, the actants who support the draft law elaborate a new system, ignoring the advances of CNS/CONEP.

The controversies raised rescue the 'slowness' and 'bureaucracy' to justify the clash on (a) how the relationship between CONEP and the CEPs will be and (b) what level of 'centralization' versus 'decentralization' will be under responsibility of these actants in order to make the procedure faster and safer.

'Centralization' favors the agreement of the system, which would act in a more homogeneous and cohesive way, but risks to delay matters that get stuck in a single body. 'Decentralization' tends to speed up the process, but generates the risk of system fragmentation, as each CEP will give its own interpretation to the rules of the system without guaranteeing uniformity to the decision criteria.

The "CONEP+Jorge Venâncio" network takes advantage of the opportunity to defend the formula applied in Resolution 506/2016 ('decentralization' with 'agreement'), to criticize the proposal to create a law (whose generalization would lead to fragmentation):

> Our idea is to decentralize, but keep the system in agreement, without making a process that creates a mess. When putting up a relatively generic law with 700 committees to construe it individually, with no one conciliating this system, this tends to generate a few hundred different interpretations. We must decentralize, but adjusting all decisions. (CONEP - Jorge Venâncio, CT0201 P01 d, on 11/10/2015)

In defense of PLS 200, the body of agreement of the system, be it ANVISA or CONEP (under the control of CNS or the Ministry of Health) is reaffirmed, and the Indian experience is also invoked to reject complete decentralization once and for all :

> "The attributions [of CONEP] are here, Senator: formulation of guidelines, technical standards, parameters – because that's what India lacked. They decentralized everything, and the situation was hopeless.
>
> You need to have a Conep above the entire system to conciliate, but it doesn't have to redo work that has already been done in CEPs; however, someone has to say: "this CEP is free to evaluate any type of project. (ICESP – Paulo Marcelo Hoff, CT0201 P01 d2, on 11/10/2015)

The survival of an ethical regulation of "dual instance", with no overlapping and reconciling 'decentralization' and 'agreement' was the choice of the networks that acted in the committees that operated in the Chamber of Deputies.

The opinion text approved by the CCTCI makes this clear when it separates the attributions of the "ethical analysis body" (article 2, item XXIV, PL 7082/17) and those of the "national clinical research ethics body" (article 2, item XXV, PL 7082/17):

> “The proposal establishes two instances, one national and another local, each with functions defined in the law and that do not overlap. It will be up to the national instance to carry out the normative and administrative functions, as well as the second deliberative instance of ethical analysis processes, in the event of an appeal against the decision of the Research Ethics Committee (CEP). In turn, the evaluation of ethical review processes will be concentrated in CEPs. (text of the opinion of the CCTCI rapporteur, approved on 12/18/2017).

The CCSF maintained the CCTCI proposal, but the CCJC made changes to the list of competencies of CONEP, motivated by the search for "speed in the analysis of strategic clinical studies for the SUS and allow greater representation of the participants of research in the CONEP Plenary” (opinion number 5 of the CCJC, approved on 06/02/2021).

The alteration of the CCJC represents a performative effect of Resolution CNS 506/2016, since in sub-amendment number 07, approved by this committee, what is verified is the recognition of different levels of clinical research, and CONEP being assigned the competence of "single instance" to:

> “(...) ethical analysis in cases of research considered of strategic interest to the Unified Health System (SUS) by the Ministry of Health”. (new text given to article 8, item VII of PL 7082/2017, approved on 06/02/2021)

Meanwhile, CONEP, which criticizes the Bill, maintains denounce of the system's decentralization and of the retrogression towards the interests of the research participants. The network lists "Phase IV of clinical research" for "endorsement" of its argument.

According to item XXXI of article 1 of PLS 200/2015, in its original version, "phase IV of clinical research" is the observation study, also called 'pharmacoepidemiological', post-registration or post-marketing, in which there is monitoring of patients with a certain pathology undergoing treatment with a new drug or product marketed in order to assess therapeutic strategies and monitor the emergence of already documented adverse reactions and those not detected in previous phases of clinical research.

Article 12 of PLS 200/2015, in the version presented to the CCJC, proposed that:

> Art. 12. In case of phase IV clinical research, the documentation required for the ethical review process will be determined by the CEP or CEI to which it is submitted.

For the "CONEP+Jorge Venâncio" network:

> “The project practically releases Phase 4 projects from ethical review [Phase 4 refers to projects after the drug is already registered]. It states that each Ethics Committee is free to define what documents will be requested in the analysis of Phase 4 projects, and assumes that a Phase 4 project is a risk-free project. (CONEP - Jorge Venâncio, CT0202 P01 b2, on 11/10/2015)

Medicines which caused adverse after being registered and marketed are also mentioned, reinforcing that the decentralization of the ethical instance in phase IV of clinical research would compromise the safety of users of these medicines:

> It was exactly in the Phase 4 research that some of the biggest problems with medicines in the world were discovered: thalidomide, vioxx, and so on. Therefore, this idea that Phase 4 research is risk-free seems unrealistic. (CONEP, Jorge Venâncio, CT0202 P01 b2.3, on 11/10/2015).

Article 12 of PLS 200/2015 was deleted, eliminating the possibility that the ethical control of phase IV was attributed exclusively to CEP's.

d) The composition of the CEP-CONEP system - CT02.04[32]

Finally, after defining "who is in charge" in the system, both in CONEP and in CEPs, and on how the bodies interact in order to offer "speed" and avoid "overlaps" in their analysis instances, the networks face controversy regarding the composition of the members of the system.

The subject is sensitive, as it rescues the participation of democracy, which was an actant that intermediated several translations in the remodeling of regulation; it also involves defining the practices and power relations of the actors-networks that mobilize; finally, it silences other actors in pursuing the disputed interests.

The controversy surrounding the composition of the system involves both the national instance of CONEP (which will act in the regulatory, appeals, and directly in exceptional cases) and local instances, of the CEPs (which are the ones that will effectively deliberate the protocols of clinic research).

> "As for the composition of the National Research Ethics Commission, it makes a qualitative change in relation to the current composition. What is the current composition of CONEP? There are 30 members, 22 nominated by CEP's, 8 nominated directly by the Council, according to the Council's boards, 4 nominated by users, 2 nominated by health professionals, national entities, and 2 by the Ministry. What does PL do? It reduces substantially the participation of Ethics Committees.
>
> I was saying something important: that the members of Ethics Committees are chosen by a parity commission: half CONEP, half Ministry. What happens? As no one has a majority in the Commission, it is only decided by consensus. This has resulted in the participation of the best of Brazilian universities at CONEP: rectors, pro-rectors, deans, people with the highest technical qualifications. There are 22 of the 30 members. (CONEP, Jorge Venâncio, CT0204 P01 e, on 12/06/2018).

[32]Link of the Map of Controversies CT02.04: https://bityli.com/74QxrC

At the national level of CONEP, the discussion on the composition of this committee only takes place from the moment it is resurrected by the CCTCI, already in the course of the work of PL 7082/2017, since before that CONEP was not even covered by the PLS 200/2015.

And it was at CSFF, already under PL 7082/2017, that the operating structure of CONEP was defined as follows:

> Art. 10. The CONEP Plenary will be interdisciplinary and independent and will consist of 15 (fifteen) members representing the following bodies and institutions:
>
> I – 10 (ten) representatives of Research Ethics Committees – CEP;
>
> II – 1 (one) representative of the Ministry of Health – MS;
>
> III – 1 (one) representative of the Federal Council of Medicine – CFM;
>
> IV – 1 (one) representative of the National Health Council – CNS;
>
> V – 1 (one) representative of research participants;
>
> VI – 1 (one) representative of the Brazilian Society of Bioethics –SBB.

Submitted the CSSF PL 7082 to the CCJC, the battle for greater representation of research participants began to increase. On the other hand, the technical group managed to get a vacancy in the CONEP collegiate body for the Ministry of Science and Technology.

> "Art. 10. The CONEP Plenary will be interdisciplinary and independent and will consist of 17 (seventeen) members representing the following bodies and institutions:
>
> I - 10 (ten) representatives of Research Ethics Committees (CEP);
>
> II - 2 (two) representatives of the research participants;
>
> III - 1 (one) representative of the Ministry of Health (MS);
>
> IV - 1 (one) representative of the Ministry of Science, Technology and Innovation (MCTI);
>
> V - 1 (one) representative of the Federal Council of Medicine (CFM);
>
> VI - 1 (one) representative of the National Health Council (CNS);
>
> VII - 1 (one) representative of the Brazilian Society of Bioethics (SBB).

At the local level of CEPs, network movements used social control to legitimize the interest in protecting clinical research participants, but in practice, this translated into introducing other actants into their compositions, such as gender-based representations and indigenous population.

This is what was approved in Amendment 2, by the CCJ of the Senate, when they established that the CEPs would have a “multidisciplinary composition and gender balance”. There was also sub-amendment 10 (to Amendment 2) which proposed that the ethical body would have “a consultant familiar with the language, customs and traditions of the specific community when the research involves an indigenous population”.

Amendment 2 was incorporated by the CCT in the substitute text approved by Amendment 22, but sub-amendment 10 was rejected.

As PL 7082/2017 was considered by the three committees of the Chamber of Deputies – CCTCI, CSSF and CCJC –, on 11/24/2021 it received a request to include the agenda to be considered by the plenary of deputies. If approved, the project will be returned to the "Initiating House (Casa Iniciadora)" of the Federal Senate, where the actants will certainly keep the black box open around the regulation of clinical research that follows its path of reassembly and performativity.

09 REGULATION AS A PERFORMATIVE PROCESS

In this section I present the analysis and discussion of the narratives described in the previous chapter.

The organization of analysis follows the same proposal used by Villar (2019) who researched the decision as a performative process, in his doctoral thesis.

It is an analysis that makes use of abductive logic, but which does not have a specific theorization, as in the work I consider the Latourian perspective, which is more focused on the description of the relational process than on a cause or consequence of this dynamics.

On this thesis, the proposal consists of analyzing the narratives constructed from the cartography of controversies articulated with the theoretical framework adopted in the thesis.

Then I organize the analysis according to the following subsections: in section 9.1 I analyze the disputes of interests involved in the process; in section 9.2 I present the main actants mapped in relational networks; and in section 9.3 I describe how actants relate to produce, alter and stabilize the researched reality.

9.1 Controversies involved in the process

In an actor-network view it is necessary to live with process, uncertainty and the constant flux that produces a becoming reality that shapes itself dynamically.

In this aspect, it is interesting to notice that the identification of a controversy is in itself a reduction of this reality, since in relational dynamics the agentic elements give rise to movements that the observer is not always able to follow or identify.

It is worth to mention that the very identification of the controversies described in the narratives has a performative character that points out reality from the observer's lens and according to the limits of access obtained for carrying out the work.

Had there been the opportunity for an ethnographic or even an ethnological approach – as Latour did in the years he attended the French Council of State to produce his magnificent work “La fabrique du droit” (2002) –, the results would have been more detailed and influenced by the capture of several other controversies that were certainly present in the relations developed along the process of regulatory reassembly of clinical research, as analyzed.

I also observe that in an ontology of in flux processes, reality has a dimension of continuity where one could not establish initial or final terms for its understanding. I made choices and did so pressed by the temporal-spatial limitation assumed in the analyses.

Regulation is an artifact that transcends the frameworks assigned to it in section 3.2. Clinical research, as well as the ethical concern involved in it, is a hybrid that retrieves relational elements from the very conception and development of health, as analyzed in section 4.1.

On the other hand, I emphasize that the shorthand notes used as a basis to map controversies have their wealth and served the purposes of the thesis. The idea of following the work of actants in the course of a legislative process has a unique meaning that crowns what Latour (2007) considers a perfect environment for identifying controversies. Where else could I identify with such clarity and deliberation the clash, the pressure, the conflict and the struggle for interests, if not in a legislative house?

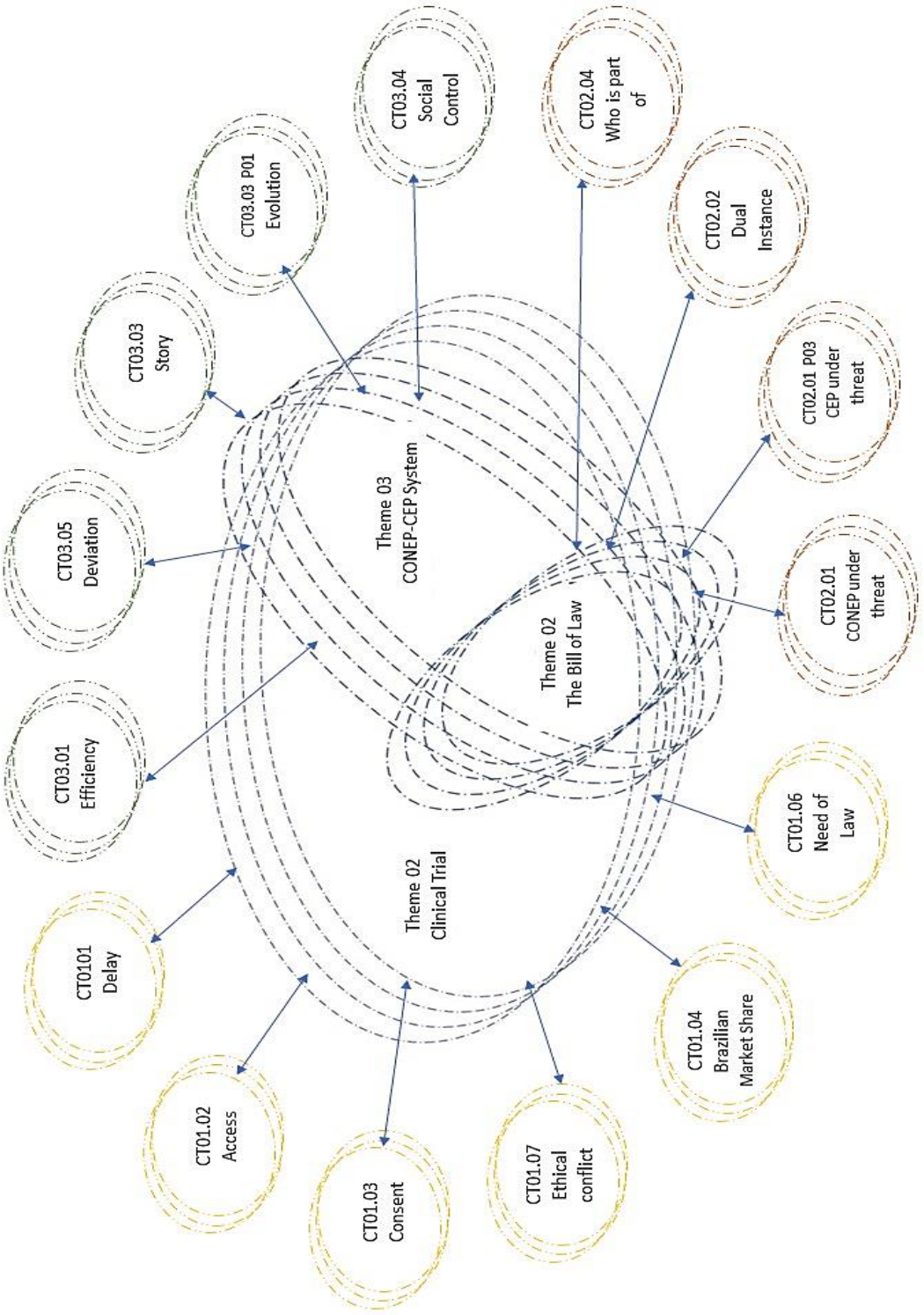
And I observe that far from moving away from the interest in the organizational-theoretical mainstream, but giving rise to the heterogeneous focus of the research, what has been proposed here involves the investigation of an “open and close” of black boxes within what I call a large “resonance box”, in which the most diverse interests (from pharmaceutical organizations and CRO's going through scientific communities, patient groups, research participants, and even regulatory authorities) were present.

Such actants, accompanied by non-human elements active in the process, were represented by (human) parliamentarians and (non-human) legislative artifacts, all of whom acted in what I call the "arena" of controversies: the legislative process known as PLS 200/2015, which was renamed PL 7082/2017.

Thus, the stage known as "sampling" of the process of mapping controversies (TURETA, CLEGG, 2021) resulted from the author's observational work in search of performative friction points, as actants manifested conflicting interests around the central issue that guided the interface of 'regulators versus regulated' relations: the conflict between agility and safety in clinical research activities.

The ramification of the controversies was organized in “Popperian trees” (VENTURINI, 2010b), respecting the unfolding and complexity with which the networks were developed. Thus, in a structure prioritized by themes, positions and arguments, a summary of the controversies can be seen in Figure 19, below.

Figure 19 Controversy Map:



Source: the Author

9.2 Actants involved in the process

In the procedural-relational approach adopted in this thesis, I do not see actors as substantive realities, but as actors-networks or relationships arising from the association between human and non-human actors, whose participation is planned, horizontal, diffuse and dispersed. In a word: rhizomatic.

In my thesis I only refer to such network-actors as actants, as it occurs in ANT. Here, the terms 'actors', 'network-actors" or 'actants' were adopted interchangeably, as ontologically processual and relational agents.

Among the different types of participating actors that mediated the regulatory deconstruction and reconstruction process, I could observe the prodigality of macro-actors or institutional actors, which are collective aggregates constituted by punctual relations and that, for this reason, externalize reified relational patterns.

Although such macro-actors appear in the narratives as supposedly ready-made or given entities, they are actually collective aggregates in formation whose supporting networks have their own translative and performative dynamics.

The macro-actors took different positions in the process, guided by the relational arrangements that supported them. The participation of macro-actors occurred through the speech of humans, whose vocalization was also the result of their associations with other actors, able to produce effect in “reassembling” the regulation.

The table below outlines, for example, the description of some of these macro-actors in the process:

Table 7 role of macro-actors in the regulatory reassembling

Macro-Actor	Source	Evidence
CONEP, vocalized by its president Jorge Venâncio	CT 01.01 CT 02.06	CONEP response time decreased from 10 to 11 months to 48 days. This idea that there are still projects taking a year or a year and a half is completely unrealistic at the moment. Here are the links to all these articles and also to some articles against the project – from Cebes, Abrasco (Brazilian Association of Collective Health), Brazilian Society of Bioethics, the UNESCO course here in Brasília and, finally, the Latin-American Federation of Ethics Committee.
ALIANÇA BRASIL, vocalized by Fábio André Franke	CT 02.05 CT.02.06	A Group was created to study the need of a bill to regulate clinical research in human beings. It has already gone through several instances. After this time, nothing has changed for patients from a practical point of view. I represent Aliança and researchers, patients and all research workers who have no chance of participating in medical science opportunities, as the most developed nations do.
FIOCRUZ	CT01.06	In many aspects, the proposals presented by Fiocruz are very similar to the current resolutions of the National Health Council. I believe that it would be better if some of them remained as resolutions and did not become part of law.
SENATE	CT 01.06	I think it would be important for the Senate, the National Congress, to endorse the National Health Council as the body that regulates these details of the process.
RUSSIA	CT0104 P01 b1	“Russia is not a model to be mentioned here. Russia is a model for doping athletes to win a competition! We have to compare comparable things!

Source: the Author

In the highlighted excerpts, it is possible to observe that the dynamics of macro-actors is always produced by relational interactions with effects on the process of regulatory deconstruction and reconstruction.

Notice the effort of CONEP network to demonstrate the reduction in deadlines for analyzing clinical research projects. Observe the search for endorsement, both by CONEP and by ALIANÇA, from other macro-actors, aiming at lending credibility to their actions. When the actant ALIANÇA states that “several instances have already moved on”, I recognize here the participative nature of CONEP's performativity, which becomes a mediator of the vocalized agency itself, regardless human voluntarism. I also observe how CONEP tries to mobilize FIOCRUZ and the SENATE to support the preservation of the regulatory status that PLS 200/2015 seeks to restore.

The agency, in addition to the participation of humans and institutional-actors, also involved a set of non-human elements that we classify as (a) objects, (b) quasi-objects and (c) artifacts.

The nature of relational and hybrid formation of these actants was presented throughout the narratives, but here I emphasize the performative aspect of these elements as they entered the networks of relationships.

The presence of these elements in the reconstruction of regulation can be perceived by the influence they had throughout the conflicts, to the point that without such elements, the development of reality would be different in the relational course.

The table below illustrates some of these objects, quasi-objects and artifacts.

Table 8 Objects

Non-human element	Source	Evidence
Phospho-ethanolamine pill (object)	CT0304 P01	We cannot mix ideology with science or mathematics. It is a precise issue and researchers know it. That's what we're dealing with: the pain of thousands of families who strongly manifested when the controversial cancer pill was discussed because everyone has an urgent need to cure patients.

Source: the Author

One of the first critical manifestations to the regulatory artifact that was proposed throughout the legislative process was the mediation of the well-known "cancer pill", whose agency was decisive not only to open the black box that culminated in PLS 200/2015, but also to act at times when elements such as “hurry”, “agility”, “efficiency” and “fight for life” were manifested in the network works.

Likewise, the texts, which are documents in the form of reports and legal opinions, were actants that gave resonance to the decisions of the bill, and were important in the struggle of disputed interests around the reassembly of the regulatory artifact.

Table 9 Documents

Non-human element	Source	Evidence
“The Times of India” (document)	CT0103 P01 b	“The parents of these girls weren't even aware that they were part of the research and were getting an experimental vaccine. Perhaps the independent Ethics Committees thought that vaccination, as part of a Phase 4 clinical trial, was not a substantial risk and that it was therefore enough to get the consent of the owner of the inn where they were staying, rather than getting in touch with the girls' parents, who could be illiterate and therefore unable to understand the nature of the research. Or maybe they thought that approaching parents, asking for consent for the HPV vaccine, could be culturally inappropriate and problematic as it involved sexual activity among adolescent females, which is a taboo subject in India, and would mean that the parents would not be willing to give such consent" (excerpt from the article published in the Times of India, CONEP).
Legal opinion (document)	CT 0106 P01	In this regard, we reproduce here the opinion of the jurist Luiz Roberto Barroso, current Minister of the Federal Supreme Court, who quite clearly stated that (...).

Source: the Author

The texts can be the result of oral conversations or be in written form. In the present case, from a process conducted by essentially formal legislative activity, I emphasize the agency of documents that gained a punctuated character as they began to be repeated and used in other moments of conversational interaction, in the form of stylization, such as happened with the report on the experience of Indian regulatory review and with the legal opinion of the Minister of the Federal Supreme Court, Luiz Barroso.

These documents supported the arguments of the actors-networks and were part of the action throughout the process.

It was also interesting to observe the de-contextualization promoted by the documents, as their actions were translated and renegotiated in different spatiotemporal situations in which they were presented.

This was the case, for example, of the opinion of 'Luiz Barroso-minister' that was given when he still was 'Luiz Barroso-lawyer'. After being made a 'minister', his decisions at the Federal Supreme Court conflicted with the legal position issued when he defended the need of a law to provide legal certainty to the regulatory artifact.

Facts also played a role in the relational process. These are episodes, events, phenomena or situations that cannot be understood ontologically as persons or objects, although in ANT they can be taken as subjectified or objectified entities.

Table 10 Facts

Non-human element	Source	Evidence
Cancer	CT0101 P01	Someone who has cancer cannot wait – cannot wait! I am deeply sorry. Other people of the same age and with other types of cancer did not have the same privilege [as Adolfo Hass] of having entered the research. What happened? They died! They died because they did not have access to clinical research. And that's what we're, in a way, doing when we're slow to vote on a process of this nature: letting people who have cancer die, waiting, at the door of hope, for research that can give them survival. And I'm sorry, Senator Vanessa, for this request for a view because we're going to have to a delay of one more week in a matter of this nature
Blue November	CT0102 P01 c	Yesterday, per my request, we did a “blue November”. What for? In order to prevent and draw attention to prostate cancer. And, during the public hearing broadcast throughout Brazil, do you know what happened? A retiree, a public servant from Betim, Minas Gerais, called to say the following: "Senator Ana Amélia, it's no use campaigning for prevention. For 18 years I've been asking a public system to have a prostate exam. 18 years! And I just can't have this exam done.
Joelma Building	CT01.07 P01 a	Joelma building was on fire. Those people didn't throw themselves out of the building because they wanted to, but because it was the only alternative they had to save their lives. If I'm going to burn to death, I might think, "I'm going to throw myself off the twentieth floor, and maybe something will happen, and I'll end up surviving this tragedy.
“Have the fox looking after the hen house”	CT0103 P01 c	“Sometimes, in an effort to solve a problem, we have the fox taking care of the hen house. If we do not pay attention to details, especially in relation to private autonomy, to the manifestation of the will of all sectors, we run the risk of putting the fox to take care of the hen house.
“Look for problems”	CT0305 P01 d	We're not trying to prohibit something unnecessarily. That’s definitely not Conep’s idea. We are trying to make the most of everything that is proposed in order to do something that is beneficial to the research participants. That's the mind we're working with. So, it must be clear that we are not looking for problems.

Source: the Author

Cancer is a chronic disease that inevitably takes on a subjective character: “cancer is ending my life”; “I live with cancer”.

"Blue November" is an objective program promoted by SUS to alert the male population to early diagnosis of prostate cancer. Both the disease and the educational event enter the network to join the other actants in defense of the bill, also generating the performative effect of changing the regulatory artifact in its infra-legal instance.

The fire of the “Joelma Building” was a tragedy that occurred on February 1st, 1974, in the central area of the city of São Paulo, Brazil, which caused the death of 187 people, left more than 300 injured and is remembered by Brazilians as a synonym for tragedy, situation that was carried over to the death of patients with cancer who are not benefited due to the delay in clinical research. The rescue of this episode enlisted an actant that relativizes the search for “safety” of participants of clinical research in favor of PLS 200/2015.

Finally, anecdotes were also stylized to emphasize vested interests behind the reassembly of regulation, as would be the case of economic interests represented by research sponsors in deregulating clinical research, or reaffirm that CONEP would be willing to collaborate with the rebuilding of the system.

I also identified the participation of concepts in the composition of regulation. It was given a new meaning thanks to the conceptual attribute that it would be “bureaucratic”. On the other hand, the notion of “consent” influenced the extension and direction of the power that would derive from the regulatory relational arrangement under construction.

Table 11 Concepts

Non-human element	Source	Evidence
Bureaucracy	CT0301 P01 g	“First, the approval of CEP from abroad and then from a local coordinating CEP; then it is centrally approved by Conep; then it goes back to the local CEP appraisal; later, we need to wait for Anvisa's approval; and finally, we have to wait for the product to be imported. This time exceeds a year on average. What happens in practice? There are 700 CEPs throughout Brazil. There is a need for a second centralized approval. With each new questioning, the period of 30 to 60 days is renewed, which, depending on the pending period and resources, is even longer, causing the delay and the process to get stuck.
Free and informed consent	CT0103 - P01	This need came from abuses that took place during World War II. There was a whole international debate about these terrible experiences, and there emerged several norms whose main concern is to protect research subjects, especially with regard to their autonomy and the need to obtain the subject's free and informed consent to participate in the research.

Source: the Author

Several artifacts participated in the process of remaking the regulation, also considered an artifact or hybrid of socio-technical relations. Shorthand notes record the presence of indicators, videos, slides, spreadsheets and indexes, but here I highlight the indicators and norms that acted performatively in the process.

Table 12 Artifacts

Non-human element	Source	Evidence
Clinical trials government (NIH)	CT0105 P01 x	Let's look at the picture of the rest of the world. Brazil is in fifth place; Canada in first; China in second; Korea; Israel; Brazil the same as Israel; we have recently surpassed Australia, we are ahead of Japan, the third largest economy in the world, we are ahead of the other BRICS; Russia; India; in front of Mexico; in Africa, the first country is Egypt, and ahead of Argentina
Internal Regulations of the Senate and Chamber of Deputies	CT0101 P01	Senator Vanessa, I am sorry for the request for a review because we're going to have a delay of one more week in a matter of this nature.
Resolution CNS 506/2016	CT0303 P01 b	In the current model [Resolution 466/2012], the protocol goes first through the local CEP and then to CONEP when the risk is high, and then to the participating CEPs. Like the new model [Resolution 506/2016], the protocol goes directly to the accredited CEP, and then the local CEPs would only check local issues, which generally have a fairly quick processing. With this, the analysis period can be reduced to something around 30 days within the accredited CEP.
International norms as the Nuremberg Code and the Declaration of Helsinki	CT 0106 P01	The international regulatory instruments for clinical research with human beings were edited precisely to give greater protection to research subjects, the most vulnerable side of the relation. The Nuremberg Code and the Declaration of Helsinki, for example, presuppose that the advancement of science is not an absolute value and must respect ethical values and human rights. All this to prevent abuses against the dignity and integrity of people, as has already occurred in dark moments of human history, such as the experiments the Nazis carried out with Jews and other groups
Federal Constitution	CT02.01	The bill does not create an executive branch, because if it did, it would be unconstitutional due to a flaw in the initiative. In order to avoid such failure, and aware of the regulation of the subject, the text of the Senate defined instances of ethical analysis in clinical research, which is perfectly compatible with the Federal Constitution.

Source: the Author

The restoration of credibility of the CEP-CONEP system was achieved thanks to indicators that highlighted the relevance of Brazilian clinical research in the world scenery. Changes advocated by PLS 200/2015 (PL 7082/2017) were avoided when international standards reminded the networks that were references to the construction of the infra-legal system that was intended to be deconstructed. The resolutions of CNS, created after the

beginning of the legislative work, are perhaps the best example of the performative effect generated in the intra-relations of the regulatory artifact. Additionally, the Constitution of the Republic revived CONEP, bringing it back to the system, although reconfigured.

9.3 The inter and intra-relational performativity of regulation

In this section, I analyze what in the cartography of controversies is called “tracing” (TURETA, CLEGG, 2021) or the understanding of how actors-networks relate, connect, disconnect and achieve alignments, generating translations.

In this respect, some decisions, even if not definitive (since they are subject to review by each of the legislative commissions that considered the project), were punctuated in the form of approval of amendments and opinions described in narrative number 03 from the previous section.

I also emphasize as a "labeling" of the mapped movement that the relationships arising from the actants who remounted the legislative process acted simultaneously inside and outside the National Congress: while a bill struggled to become a law, the regulatory artifact produced its improvement to harden itself and try to prevent the advance of the bill. The performativity of the elements at stake was therefore bidirectional.

I would add that not only did regulation generate and suffer performative effects in its own reconstitution, but it also promulgated realities in its relation with the activities and entities subjected to it, such as the formation and existence of CROs, formation of groups articulated around PLS 200/2015, as was the case of Aliança Brasil, besides the decision of the pharmaceutical sector of directing its activities to other countries, as recorded in section 4, in which I analyze the clinical research segment

I call such phenomena performative effects that occur in intra and inter-relational ways and are guided by the three rhetorical questions below.These questions were also formulated with inspiration from the model suggested by Villar (2018) in his thesis on decision as a performative process:

a) What is regulation?

The socio-material notion derived from ANT allows us to move regulation away from the notion of an institute resulting from deliberate human will, to be understood as a negotiated process of heterogeneous interests whose agency is symmetrically distributed.

It is also the effect of an agencement (socio-technical arrangement) whose network-actors claim power over the other actants who participate in the network.

Therefore, although the artifact is valued for its controlling and limiting attribute of the action of entities subject to it, the relational view allows us to see regulation as a negotiating space to distribute power where relations arising from the actants assemble and remount the reach or the extent of the networks that configure the artifact.

b) How is it constituted?

As I could see from the performativity of the actants, the regulatory artifact is punctuated to assume a reified form of institutional actor (for example, the CEP-CONEP system) and lists other actants such as, "ethics", "risk" and “democracy” (in its variations) to sustain the acquiescence of the other actants to control the relations that constitute the regulatory artifact.

There is no power of the actors-networks that constitute regulation without the silencing of the actants of the network that associate around the regulated activities.

In this sense, the struggle of the elements regulated by the control over the assemblage of regulation highlights the power of the regulatory artifact, whose source is based on the associations of networks of regulated actors.

In this dynamics, other actants are called to join the network (science, the legislative process, diseases, economic interest etc.) in a continuous struggle for mobility and extension of power that circulates relationally through regulation and regulated activity (clinical research) .

c) What are the movements or the trajectory of this process of constitution of the regulatory artifact?

Regulation is an eminently procedural artifact, regardless of its highly punctual aspect, which is manifested by the production of normative relations.

There is a fluid action of relational elements, which act to endow it with apparent reification. However, when there is the subsumption of the relations that regulation supposes to control, it is also affected by the several possibilities of reinterpretation and consequent reassembly of its own assemblage.

Therefore, the procedural nature of this movement occurs either through the intra-relational mode in a bidirectional sense or through the interrelational mode in relation to the elements to which it is subsumed.

The intra-relational movements involve the activities of the network that go back to the regulatory agencement, both in the legislative process and in the infra-legal scope.

Interrelational movements involve the associations that the regulatory artifact maintains with the elements that integrate the set of relations that punctuate the entities subject to regulation (clinical research participants, sponsors, scientists, for example).

Here I go back to an interesting debate on the controversy surrounding the need for regulation of the macro state actor and, if it is necessary, I ask once again: what, why, when, where and how to regulate.

The antagonism and polarization of controversies glimpsed in clinical research served to demonstrate that regulation is nothing more than an artifact to point out the power of networks voiced by humans, non-humans and macro actors involved in it.

The position of an actor-network manifested by its interests and by the combat of its opponents is determined by the socio-material relations that support the network to which it is associated.

Therefore, polarizations, antagonisms, conflicts and controversies are functions of sociotechnical networks that mediate these associations. Constituent elements of these networks are positioned “against” or “in favor” of a particular interest depending on the relationships they are involved in within the networks in which they participate, which aggregate and disaggregate, procedurally and performatively.

Controversy and performativity of relational networks, initially antagonistic, generate spaces for negotiation or a zone of translation, through which they pass and establish contacts with new constituent elements of networks.

It is from these movements that we can perceive the translation, the displacement, the reassembly, the closing of black boxes and the punctuation of relations that are reified in what we see as a regulatory system.

It is also interesting to notice that the discussion about whether regulation is necessary or not, or what levels of regulation are involved in the different regulated activities, could be re-signified if we adopt the relational, socio-material, procedural and performative approach.

Perhaps this controversy in itself becomes an adiaphora, since ideological, political, economic or social factors would no longer serve to justify antagonistic positions, but would become integrated into the networks to be also performatively reassembled from the relationships in which they are immersed.

In this sense, regulation will always be present in the work of networks, whose power will always be explained by the associations of human and non-human actants attached to it.

A law may or may not be passed, infra-legal norms will emerge and pass, microorganisms will fight for their survival, scientific knowledge will advance (breaking or not their paradigms), States and organizations will voice the interests of those who circumstantially integrate them, and even objects, documents, facts and artifacts will tell, in their own time and manner, how the relationships that weave the performative mosaic of regulation will be packaged.

10 FINAL CONSIDERATIONS

In this thesis, I tried to analyze the meta-organizational regulatory dynamics involving an ontologically flexible approach and employing a performative mentality that would allow a glimpse of action from a post-human and socio-material perspective.

With regard to the objective of conceptualizing regulation, based on the experience of Brazilian clinical research, under a processual-relational ontological perspective, it was possible to understand regulation as a relational process whose spatiotemporal movement is standardized, generating stabilization of networks, at the same time that it raises controversies that generate displacements (translations) that act performatively on the relations arising from actants that acquiesce to regulatory power (clinical research), as well as on actants that punctuate the regulatory agencement itself (CEP-CONEP system).

With regard to the objective of discussing regulation, as an agencement or socio-technical arrangement arising from the work of heterogeneous networks acting on clinical research, and which at the same time has been discussed in the context of a legislative process underway in PLS 200/2015 and PL 7082/2017, in its procedural and performative aspects, we found empirically that regulation constitutes and is constituted by relationships mediated by heterogeneous elements of networks that coexist symmetrically. Both the regulation (actant) and the process that defines the object of regulation (regulated activities) generate effects and suffer performative effects in relation to other actants or heterogeneous elements (human and non-human) that make up the networks.

In regard to the objective of spreading the cartography of controversies as a technique that allows the description of processes of constitution of moving realities, it was possible to consolidate the contributions of Venturini (2010) with the recent works of Tureta and Clegg (2021), generating a proposal of operationalization of relations between actants that combined 'dispute' and 'negotiation', reassembling reality in a performative way.

I also highlight the contributions generated through the thesis, which I subdivide into theoretical, practical and methodological contributions. As for the theoretical contribution, on how performativity is verified from the intra and inter-relations that constitute the regulation of Brazilian clinical research, predominantly associated with a static and stabilizing phenomenon, but which in this thesis was understood as a relational and procedural artifact, I could observe that regulation controls, but is also controlled by actants that constitute the punctuated networks and reify regulation. It is in these performative movements of power and control that clashes are established and who is in control and extent of control are defined.

Even upon the clearly normative character of the regulatory artifact, the attribute of dynamism is present in it due to the possibilities of subsuming regulation to concrete cases in which the rules are applied.

It was possible to notice that even upon perception of apparent stabilization of the regulatory artifact, the "black boxes leaked", borrowing the expression of Latour and Callon (1981), so that at any time the relations were able to promote reorganizations in the networks that supported the CEP-CONEP system.

In this sense, the legal framework recommended by the current PL 7082/2017, still in progress, would not be the one that would put an end to the infra-legal regulatory model built under the aegis of the CNS. We are facing a negotiated process of translation of relations that remains ontologically unfinished, acting and being performatively influenced by human agency, objects, artifacts and their associations.

And it is in this aspect that the practical contribution of the thesis resides. I do not foresee stability in the regulatory reality, but the multiplicity of realities that overlap and combine to support the dynamics.

Such realities, supported by relationships that define their positions (such as the sectarians of efficiency as opposed to those who defend safety in clinical research), transact their interests and mutually interfere in the constructive trajectory of the regulatory artifact.

Perhaps, thereby, the impossibility of prescribing evaluative judgments that prescribe "who is right" about existential controversies is recognized, since we would also be inexorably inserted in the relations that take part in the networks that act performatively on such realities.

By taking a stand, we also become actants and enter the process that follows its path despite our intentions, but influenced by our relationality. The observation of this fact makes us reflect on how mitigated our expectations about voluntarist, causal, rationalizing pretensions based on human exclusivity should be.

From a procedural-performative view, considering relationality and socio-materiality as a presupposition, I understand that the description precedes the explanation, just as stated by the ANT theorists, especially the Latourians.

The process of following the actants in their relational dynamics, based on controversies, is what allows for a more consistent view of the constitution of reality, without the modernizing addiction of taking for granted what still needs to be understood. Such procedural-performative posture may contribute to reduce the rush of hasty diagnoses about black boxes that never close, or at least, in which closing is not a definitive process.

Such reflections from this view enable us to recognize that the relativization of human intentionality is also reflected in a way of finding natural the performativity of network-actors in meta-organizational processes and realities, also explained ontologically by becoming, although not punctuated under the name of actor-institutional.

The methodological contribution is evidenced by the adoption of controversy cartography (VENTURINI, 2010a) as a viable technique for describing processes of constitution of moving realities, with more operable indications on how actors-networks promote translations, moving ontologically procedural realities, although often punctuated by performative effects. ANT research is very difficult and the increased use of cartography is perhaps the friendliest method to generate good descriptions of dynamic and complex processes.

As limitations of the research, among the many possible ones, I highlight the precariousness of access to a larger number of actants involved in the researched regulatory dynamics. It would be ideal that, in addition to the documentary analyses, based mainly on shorthand notes, I had also had the opportunity to carry out non-participant observation, or even adopt an ethnographic posture, which would offer stronger access to the process.

As suggestions for future research, I would like to go deeper into how controversies and translations could be better operationalized considering that they are ontologically procedural. It will also be appropriate to try to understand, from a procedural ontological perspective and using the performative mentality, how other organizational realities develop and are configured, such as innovation processes, agency conflicts and contractual configurations.

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